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# ARHYTHMIA OF THE HEART



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ARHYTHMIA OF  
THE HEART  
A PHYSIOLOGICAL AND  
CLINICAL STUDY

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## PREFATORY NOTE

THIS edition, which otherwise corresponds with the original text, is supplemented by some notes which have been added by the Author: these refer to several points in the literature that has appeared since his work was published, and are given as an appendix at the end of this book.

I gratefully acknowledge my indebtedness to my friend Dr. James Mackenzie for his help in my endeavour to give a faithful rendering of the Author's meaning.

T. S.



## AUTHOR'S PREFACE

THE results of previous efforts to analyse the irregular pulse have been here compiled along with more recent observations; at the same time it was found possible to make use of the latest results of physiological research in this analysis, to review the recent works on this subject and the various criticisms, and combine the whole array of facts into the compass of a single volume.

The different forms of arrhythmia are classified according to their origin into certain physiological types, and the various forms that have long been distinguished clinically are compared with these types. For the sake of clearness a preliminary chapter is given on the theory of the myogenic action of the heart on which the analysis that is given here depends.

Before this work can be of any direct practical importance for the diagnosis and treatment of cardiac disease, many questions of a physiological as well as a pharmacological nature will have to be solved. These questions are accordingly stated as plainly as possible, and given a prominent place in the book.

GRONINGEN, *July* 1903.



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# ARRHYTHMIA OF THE HEART

## CHAPTER I

### THE THEORY OF THE MYOGENIC ACTION OF THE HEART

§ 1. **The "Neurogenic" Theory.**—The view, which has recently been held as to the origin and regulation of the action of the heart, is essentially different from that which was generally taught less than ten years ago. From the process of development, through which the physiology of the nerves and muscles passed, it followed that the same mechanism was taken to be at work in the contraction of the heart as in that of all other striped muscles. Since the mechanism of voluntary muscles was the first discovered, it was natural that a stimulus, arising in some nerve-centre and conducted to the heart by nerve fibres, should be regarded as necessarily the cause of its contraction. A musculo-motor nerve-centre was assumed to exist, and endeavours were made to locate it. The fact, that the excised heart of many higher and lower vertebrates under suitable conditions is able to continue its rhythmical action for a considerable time longer, was a cogent argument for referring this motor-centre to the intra-cardial nervous system, instead of looking for it in the central nervous system.

As is well known, the entire heart-muscle does not contract simultaneously during a systole, like voluntary muscles: the different parts of the heart, sinus, auricle, and ventricle, contract after one another in a definite order. It was therefore assumed that first the sinus was stimulated into contraction from the intra-cardial nervous system, then the auricle, and lastly the ventricle, much in the same way as in the act of swallowing, where the contraction of the various groups of muscles involved in this movement is set up by nerve stimuli occurring in a definite sequence. In the same way, therefore, the cause of the regular peristalsis of the heart was referred to the nervous system.

The influence which two nerves, the vagus and the sympa-

A

thetic, are capable of exerting on the heart, was early discovered. In accordance with the above-described conception of the origin of the regular movement of the heart, it was thought necessary to look for the working-point of the inhibitory and accelerator influences of these nerves in the intra-cardial nervous system.

In this way it was possible to draw up a plan of the cardiac movements that was easily understood: a more or less independent intra-cardial nervous system produces the motor stimuli for the contractions of the heart and regulates the appropriate contraction in the different parts of that organ. The cardiac nerves, that arise in the central nervous system, have a positive and negative influence on the intra-cardial system, and are therefore in a position to change the action of the heart according to the necessities of the moment; an opportunity was therefore also given for the most varied reflex action on the heart, such as one meets with in experiment in so many different ways. The physiological and pharmacological experiments of Ludwig Traube and his school, for example, were all based on this plan, and even at the present day the effect of cardiac poisons is for the most part analysed from this conception of the heart's action. The heart-muscle would therefore be a passive instrument on which the nervous system plays: the mistakes in playing would first of all have to be referred to the player, the nervous system, although it is possible that injurious influences may also affect the instrument itself, viz., the heart-muscle.

Through the influence of the physiological researches of the last decade this theory of the neurogenic origin of the heart's action has been opposed by the view that this source of rhythmical movement is to be found in the heart-muscle itself; in other words, this action is of myogenic origin. At first this view was met by the strongest opposition from physiologists, but now it is receiving more and more attention and support, and although the controversy has not decreased in vehemence, the number of opponents has decidedly diminished, and even in clinical circles the "myogenic" theory has found more and more advocates, and has advanced very materially the pathology of the heart. With all due acknowledgment of the valuable researches of Gaskell, Bowditch, and others, it is to Engelmann that belongs the honour of having originated the new theory of the heart's action. Engelmann has re-arranged and endeavoured to explain the facts long ago discovered by older investigators such as Traube, Ludwig, Hering, Marey, and Kronecker; he has extended

Gaskell's experiments, brought together the facts previously known and confirmed by himself, and with a clear notion of his aim in view has gone a step further, without ever losing sight of the whole, even in the attempt to solve matters of the smallest detail: in this way Engelmann has already given us a deep insight into the mechanism of the heart such as has never yet been attained for any other organ.

How this new theory may be of the highest importance for the explanation and treatment of pathological conditions hardly needs any lengthy exposition. Subsequent investigations are all based on this new explanation of the heart's action. A short description of the theory is therefore given here by way of introduction. I have been obliged to give up the idea of a complete survey of the literature here, the object of this preliminary chapter being only to state the principal points of the theory.<sup>1</sup>

§ 2. The "Myogenic" Theory.—The theory, in which the myogenic origin of the heart's action is advocated, may be stated in this way that the stimulus that causes the contraction ("contraction-stimulus") is formed in the heart-muscle cells themselves, and is therefore not rhythmically conducted from the nervous system to them. The autochthonous contraction-stimulus is conducted onwards, not through nerve channels, but really through the heart-muscle cells, passing normally from the base of the heart through auricle and ventricle down to the apex, and in this way brings about the progress of the contraction in the various chambers of the organ. The power to produce the contraction-stimulus, the power to conduct it onwards, irritability, and contractility are properties of the heart-muscle cells, which have a certain relation to each other, but yet in their nature are so independent of one another that each may be changed in various ways within the widest limits. The co-operation of these fundamental properties of the heart cells, their behaviour during and after systole, produces the rhythmical movement of the heart, as one observes even when it is excised, and is capable of removing many disturbing influences. But the regulation of the heart, its adaptation to the various requirements of the body, is provided for reflexly through the

<sup>1</sup> While I was writing this chapter the *Ergebnisse der Physiologie* appeared, where Biedermann and Langendorff give a full list and critical review of the literature bearing on the myogenic theory. Any one who wishes to study the subject more closely will find information there. But all who are interested in it are most strongly advised to read Engelmann's own works.

nerves, *i.e.* through a positive and negative influence of the nervous system on the above-mentioned properties of the heart-muscle. The "myogenic" theory, therefore, regards the heart as an automatic organ, the action of which is adapted through the influence of the nerves to suit external circumstances: the heart might be compared to a regularly trotting horse, which moves of itself and knows how to surmount many obstacles itself, but yet is guided by the rider as circumstances require.

We will now consider the individual points in this theory separately.

§ 3. **Automatic Stimulus-Production.**—The statement, that the contraction-stimulus arises in the heart-muscle cells and not in the intra-cardial nervous system, caused a great sensation and met with strong opposition from physiologists. It did not agree with that experience which taught that stimuli arise in nerve cells alone, and that muscle cells contract only through the influence of stimuli from nerve cells conducted to them, or through thermal, chemical, or mechanical stimuli from external sources. This statement, therefore, does not merely concern a point in the special physiology of the heart, but it affects an extremely important question in general cell-physiology.

In an article that appeared in 1897<sup>(23)</sup> Engelmann sums up all the reasons that lead us to assume an automatic stimulus-production in the heart-muscle cells. The first and strongest reason is, that rhythmical contractions can occur in detached portions of cardiac muscle, which most certainly contain not a single ganglion cell (*e.g.* apex of the heart, portion of the walls of the vena cava in the frog's heart). For unstriped muscle cells (*e.g.* ureter) this fact was previously established. We must therefore assume at once that ganglion cells and nerve centres can be dispensed with in the production of rhythmical contractions of the heart. But by means of the more modern methods of staining it could be proved that numberless nerve fibres wind round the heart-muscle cells everywhere, and the question might be asked whether these nerve fibres do not perhaps provide the stimulus. Till a few years ago this question would have had to be answered in the negative, but according to the researches of Apathy and Bethe, who actually assign the most important function to nerve fibres, this question might again be raised. Indeed, Kronecker, in the paper which he read at Hamburg,<sup>(66)</sup> has made a short reference to this aspect of the ques-

tion. It is therefore very difficult in this case to bring forward a convincing proof, because the two elements, muscle cells and nerve fibres, cannot here be anatomically separated. Numerous strong arguments, however, support the view of Engelmann.

In the first place, it is *per se* more probable that such an important function as the production of the contraction-stimulus, which is preserved for a long time in an excised portion of the heart wall, has its origin in the intact muscle cells rather than in the divided network of nerve fibres.

But then the important researches of His <sup>(46 47)</sup> and Romberg <sup>(48)</sup> must be here taken into account, from which it follows, that in different classes of vertebrates the embryonic heart beats regularly, long before there is even any sign of a rudimentary cardiac nervous system. In the case of the selachians, bony fishes, and birds this fact has been proved with certainty. This movement can be especially well demonstrated, as I myself know from experience, <sup>(117)</sup> in the transparent ova of bony fishes (*e.g.* the ova of *Belone* and many pelagic species), and any one that has once observed the heart of the *Belone*-embryo, how it stretches on the yolk to beyond the head of the embryo, with its venous end in front, and beats rhythmically, without a single nerve cell being near it, he will be always convinced of the automatic action of the embryonic heart. It is only later that its connection with the central nervous system is formed, and hence the communication established that is necessary for the due control of the heart's action.

In this embryological development a suitable illustration of the phylogenetic development of the heart can be seen. In the first place we must bear in mind, that phylogenetically the muscle cell has developed from the "neuro-muscular" cell, and that in the lower animals nerve-function and contractility are united in the same cell. But even among the higher animals we find, that contraction-stimuli are produced independently of the nervous system, *e.g.* in ciliated cells. When Kronecker <sup>(60)</sup> quotes the *Myologische Untersuchungen*, written by Kühne in 1860, in order to prove that the movement of protoplasm and of cilia must be separated altogether from the true movement of muscle, it might be pointed out that the more recent researches of general physiology have actually demonstrated the common character of these different forms of movement. In Verworn's well-known book on

General Physiology<sup>(116)</sup> any one desirous of the information can easily convince himself of the position of this question.

The results of investigations into the function of the heart in many invertebrates are even more definite. In the most diverse orders it has been proved that ganglion cells or nerves take no part in the rhythmical action of the heart. Walther Straub has recently established this fact in the case of the aplysia, on which he expresses the following opinion (p. 527<sup>108</sup>):—

“Above all, one is not compelled to come to an agreement by setting up some theories as to the ganglion cells and their physiological significance—for none have yet been found.

“It is a fact, now established, in my opinion, by a large and sufficient number of examples, that the unstriped muscles of invertebrates in particular are capable of rhythmical action automatically and independently of any nerve cells setting up stimuli and controlling them. I consider myself, therefore, justified in assuming that the rhythmical pulsation of the heart of the aplysia is an example of the capacity for rhythmical movement in all unstriped muscle cells. In the case referred to this common property happens to take on the function of an organ.

“The hearts of the higher animals possess in their cardiac nerves an apparatus which permits of the economical adaptation of the heart's work to the increased or diminished requirements of the moment.”

But there is no fundamental difference between smooth and striped muscle fibres, or between the muscle cells of invertebrates and those of vertebrates. We may therefore really assume that the heart of a vertebrate, endowed with a regulating nervous system, has developed phylogenetically from a nerveless heart working independently and automatically. In the ontogenetic development, as His jun. has shown, we see then a faithful picture of the phylogenetic, since here too we find a stage, in which the heart is composed of unstriped fibres and pulsates regularly for days without any connection with a rudimentary nervous system.

Even if one were inclined to deny all automatic action in voluntary, striated muscle fibres, one would have to bear this in mind, that in the phylogenetic development those muscle cells, the automatic action of which is of the very greatest significance for the preservation of an important function, are bound to have retained the property of autochthonous stimulus-production unimpaired, since

the voluntary muscles may have completely or partially lost this function which has become of secondary importance for them. This view now is strongly supported by the fact that the voluntary muscle seems to have really only partially lost its automatic movement, and under favourable conditions can go into rhythmical action. The researches of Biedermann in 1880, <sup>(6)</sup> and the more recent works of Jacques Loeb <sup>(71)</sup> and others go to show that in the skeletal muscles, which otherwise react only to nerve stimuli, slight changes in the chemical composition of the fluid surrounding them may set up rhythmical contractions which arise in the protoplasm of the muscle cells.

Loeb has besides amply demonstrated that there are quite distinct ions that produce this contraction, and we shall further see later, that this fact is of great value for a fuller knowledge of the spontaneous contraction-stimulus. Biedermann's article on Electrophysiology in the *Ergebnisse der Physiologie* <sup>(1)</sup> gives a full account of the researches bearing on this matter (*cf.*, too, Engelmann, <sup>(23)</sup> p. 9). It follows therefore from what has been said that on physiological grounds it is not unreasonable to assume that the contraction-stimulus arises autochthonously in the heart-muscle cells.

This property of automatic action belongs to the entire heart, but the muscle-cells situated at the venous end possess it in greatest measure. Portions of the heart, even when excised or otherwise isolated, are capable of performing rhythmical contractions although only with less frequency. A contraction-stimulus will therefore always be formed first in the muscle cells at the *venæ cavæ*; the rhythm of stimulus-production at this point, accordingly, determines the rhythm of the whole heart, and therefore the contraction always starts at the *venæ cavæ*; and when the blood-stream has to be directed from the venous to the arterial end of the heart in order to keep up the circulation, it is easy to understand why this power of automatic action in the heart is greatest at its venous end.

A fuller knowledge of the events occurring in the heart before and during systole has been supplied, chiefly through Engelmann, by the so-called "Method of Extra-systole." A short description of this method, which has also proved very useful in the explanation of pathological irregularities in the human heart, may here be given.

§ 4. **Method of Extra-systole.**—Two very important properties of heart-muscle cells have been known for a long time. The

first is the "maximal" contraction of the heart, discovered by Bowditch <sup>(8)</sup>. He proved that the size of the contraction is independent of the strength of the exciting stimulus, and that (in contrast with the behaviour of voluntary muscle) stronger stimuli cannot produce greater contractions. In other words, Bowditch's law is this:—If a stimulus is strong enough to set up a contraction, the heart-muscle answers to that stimulus by using all the contractility of which it is capable at that moment. When the wall of the heart is stimulated, either a maximal contraction is produced or none at all.

The second property was discovered in 1875 by Marey, who proved that the heart-muscle possesses a "refractory phase," in which the wall of the heart is not excitable, or answers only to very strong stimuli. We owe our exact knowledge of this refractory phase to Marey, Dastre, and others, but particularly to Engelmann, who investigated the behaviour of the pulsating heart in a systematic manner by applying electrical stimuli to the wall of the heart in the various phases of the cardiac cycle <sup>(10)</sup>. If the heart is refractory, it does not react even to the strongest stimulus; if it is not refractory, a more or less powerful contraction, an extra-systole, is produced. This method of investigation, therefore, is called the "Method of Extra-systole."

When the heart, as it beats rhythmically, is examined in this way, it is found that the refractory phase begins shortly before the systole, and continues a short time after it. During the whole period of systole, therefore, the heart is inexcitable; after the systole the irritability and contractility are slowly restored in such a way that the longer the diastole has lasted the weaker is the stimulus required to produce an extra-systole, and the larger the contraction that follows.

These events are diagrammatically represented in Fig. I. *A* is a normal (diagrammatic) tracing of the ventricle. The refractory phase commences a little before the beginning of the systole (*p*), and ends at *a*. At this point the heart becomes again excitable for strong electrical stimuli; at *b* a slightly weaker, at *c* a still weaker, stimulus suffices to cause a contraction, and at *d* a short time before the next systole occurs, the excitability has almost completely returned, and a very weak stimulus may be employed. The effect of stimulation at *a*, *b*, *c*, *d* is represented diagrammatically in *B*, *C*, *D*, *E*, respectively. At *a*, the contractility has

been only slightly restored and consequently the extra-systole is a very small one, sometimes merely a temporary suspension of the diastole; on stimulation at *b*, *c*, and *d* the extra-systole becomes greater and greater (*C*, *D*, *E*), and at *d* an almost full systole occurs, because here the contractility has again been almost completely restored (*E*).

The extra-systole is invariably followed by a long pause of the heart, which has been regarded as a compensation to the heart for the extra work it has thus done, and as an opportunity for it to rest; it has therefore been called by Marey the *compensatory pause*. The explanation of this long pause was given by Engelmann, who showed that in consequence of the extra-systole, the ventricle is still in the refractory phase when the next physiological stimulus reaches it; this stimulus, therefore, has no effect, no contraction takes place, and it is not till the next stimulus after it that a contraction can again be produced. Thus the normal systole that would follow the extra-systole is missed; then the first

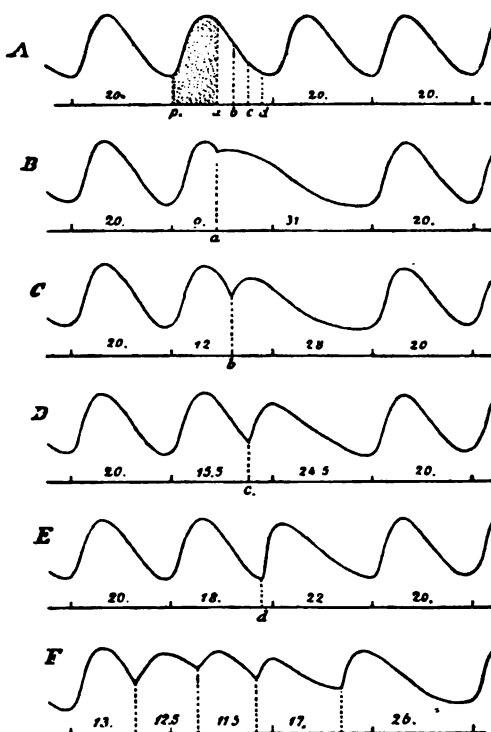


FIG. I

systole that comes after the compensatory pause ("post-compensatory systole") occurs exactly at the moment at which it would have occurred had no extra-systole preceded it. In the diagrams *B-E* the compensatory pause is also shown. It is clear that the sooner the extra-systole interrupted the diastole, the longer is the pause.

Thus the extra-systole bars the occurrence of the next following physiological systole, but in reality does not disturb the rhythm of the heart. Even after several successive extra-systoles which bar

two or more physiological beats, the first spontaneous systole always reappears exactly at the moment at which it would have occurred if there had been no stimulation of the heart (*F*). The original rhythmical movement of the heart is invariably restored, a fact from which Engelmann formulated *the law of the conservation of the rhythm of physiological stimuli*.

If the heart or a portion of its wall is not left free to reply to spontaneous stimulation, but is thrown into rhythmical contraction by being tetanised, then an extra-systole produced by a strong artificial stimulus is *not* followed by a compensatory pause, for as soon as the refractory phase is over, and the contractility of the heart is sufficiently restored, the continuous stimulation produces another contraction. This also affords a proof that the normal physiological stimulus for the auricle and ventricle is not a continuous, but a rhythmical, one, for it is only in the latter case that it is possible to have a compensatory pause.

The very highest importance must be attached to Engelmann's discovery, that while a compensatory pause invariably follows an extra-systole set up by artificial stimulation of auricle and ventricle, *this compensatory pause never occurs* after an extra-systole produced at the venæ cavæ. From this invariable result it follows with absolute certainty that the stimulus is not conducted rhythmically from outside to the wall of the venæ cavæ, the place where the contractions always commence, but arises at this very place, and is formed in a definite cycle after the systole, whether artificial or spontaneous.

§ 5. **The Nature of the Autochthonous Stimulus.**—When now we inquire further into the nature of the stimulus that arises spontaneously in the muscle cells of the heart, we must first of all solve the question: "Is this stimulus a continuous or a periodic one?" It was stated before, that tetanisation of the heart produces, not a continuous spasm, but a rhythmical movement in it. It is then impossible (except in experiments done under very special conditions) to bring the heart into tetanic contraction. This fact is explained by the refractory phase, which is peculiar to heart-muscle. For, as soon as the heart begins to contract, it becomes refractory, and is thus withdrawn from the influence of the stimulus; it is only after the systole and during diastole that the heart is again able to reply to the stimulus with a contraction. It might therefore be thought that a continuous stimulus of uniform in-

tensity is built up in the muscle cells of the great veins, where a compensatory pause does not occur, this stimulus manifesting itself in rhythmical contractions, as with tetanisation, just because at every systole the heart is at once withdrawn from the action of the stimulus. Kronecker <sup>(66)</sup> refers to this possibility, but ascribes the property of converting a tetanising into a rhythmical stimulus to the central organs. But in the case of the heart it is not necessary to accept the notion of an "increased tonus of the central organs" causing this "make and break," because here the refractory phase of the muscle itself gives a satisfactory explanation!

Now, if it were really the case that the physiological stimulus were a continuous one, that manifested itself in rhythmical contractions by virtue of the alternation of excitability and non-excitability, the rate at which the heart beats would then be dependent on the relation between the uniform intensity of the stimulus and the excitability of the organ, *i.e.* in fact, on the excitability alone. This view is advocated by H. E. Hering <sup>(41 p. 579)</sup>. Muskens <sup>(32)</sup> advanced the theory that the moment at which the stimulus becomes effective depends exclusively on the power of the heart to conduct the stimulus onwards. In opposition to this, Engelmann <sup>(22 24 25 26 28)</sup> put forward the view that the contraction-stimulus is really formed continuously, but is destroyed at every beat by the contraction, and must then be formed again anew, and this view he has managed to support by the proof that the formation of the stimulus is, within wide limits, independent of the excitability and conduction-power of the heart. The process may, therefore, be presented to our minds in the following way:—Stimulus-matter is being continually formed in the heart-muscle cells, most energetically in those situated at the venous end of the heart. When it grows to such a strength as to set up a contraction, the molecular explosion that occurs at the systole not only abolishes the excitability and contractility for a short time, but also destroys the stimulus-matter itself. After the systole, therefore, it must be built up again anew to the point of requisite strength, and the time that elapses *ceteris paribus* until this point is reached is just the cardiac cycle. The contraction of the muscle cells destroys the stimulus, whether it was produced by a stimulus from the heart itself or by one conducted to it from some other quarter. Thus it may be explained why that spot in the heart, at which the stimulus is most rapidly formed again to the point of effective strength, always gives the rate of contraction

for the whole heart. The stimulus is conducted from this spot onwards through the heart, sets up a wave of contraction in it, but at the same time destroys the stimulus-matter that has already been formed in the other parts of the organ. The most active spot then, normally the root of the heart, will always be the first to produce effective stimuli. On the other hand, by artificially stimulating any other point whatever of the wall of the heart, but at a more rapid rate than the spontaneous rhythm, it is not difficult to make the wave of contraction always start from the point of stimulation. In this way the rhythm of normal stimulation may be thrown out of action. There is therefore no essential difference in the behaviour of the stimulus in the *venæ cavæ* from that in the auricle and ventricle, such as Hering (<sup>41</sup> p. 579) puts forward as an objection to this conception of normal stimulation.

The question as to the nature of this stimulus is one of no less importance and of special interest for physiology as a whole. We spoke above of stimulus-matter; indeed, we must consider the stimulus ultimately as something tangible, material, composed of definite particles. It will probably be a long time yet before a final answer can be given to this question; while the nature of the stimulus that arises in nerve cells and is conducted along nerve fibres is also a problem still unsolved. And yet this very field of the rhythmical stimulation of muscle offers the prospect of a possible solution to this problem. Such a prospect is opened by the researches that have been made on the chemical composition of the medium in which rhythmical contractions occur even in voluntary muscle. It would go beyond the scope of this book if I went into this interesting and important chapter of the physiology of muscle in detail, and I would refer the reader again to Biedermann's valuable article in the *Ergebnisse der Physiologie* recently published<sup>(41)</sup>. I cannot, however, refrain from quoting in brief Loeb's results as they appear in his paper above mentioned<sup>(71)</sup>. These investigations throw a clear light on the principles of the myogenic theory, and open up the way for further experiments that may give a deep insight into the inmost processes of the muscle cells of the heart. Loeb's conclusions are given as follows (the italics are mine):—

“(1.) There are certain ions, *e.g.* Na, Cl, Li, Br, I, and others, which (in solution under a pressure of 4.91 atmospheres) are capable of producing rhythmical contractions in muscles. *These ions do not produce such contractions by increasing the excitability*, because (1) the

contractions continue even when the excitability is diminished ; and (2) they do not take place in solutions of non-conductors (e.g. glycerine, sugar) at the same osmotic pressure, even when the excitability is normal. *It is more natural to think that these contractions are due to definite chemical combinations which these ions form in the muscle.*

"(2.) There are ions which inhibit the rhythmical contraction of normal muscle fibres, e.g. Ca, K, Mg, Be, Ba, Sr, Co, Mn. *The inhibitory action of Ca, K, and probably of all the other ions mentioned here, does not depend on a reduction of the excitability. For on adding a very little CaCl<sub>2</sub> to some physiological salt solution the contractions are inhibited, while the excitability of the muscle is less impaired and lasts longer than it does in physiological salt solution, when these rhythmical contractions occur. It is more natural to think that the chemical combination which the ions, Ca and K, form in the muscle renders its rhythmical contraction more difficult or impossible.*

"(3.) Hydroxyl or hydrogen ions accelerate the production of rhythmical contractions when they are added in sufficient dilution to solutions of the ions that excite contractions, as enumerated in (1). But when they are put into solutions of non-conductors or inhibitory ions, they do not have the same effect. *They have, therefore, a catalytic action in the production of rhythmical contractions, but are unable of themselves to produce these.*

"(4.) From the very scanty material that is yet available it seems that only ions, and not non-conductors, have the power of setting up rhythmical contractions in voluntary muscle.

"(5.) The laws regulating the periodic action of the ventricle appear to be similar to those that have been given here for striated muscle.

"(6.) In all the experiments that have been described here *it is the muscle substance itself that sets up this rhythmical action, since periodic contractions cannot be started from either the nerves or spinal cord through the solutions mentioned in (1).*"

These results of Loeb give us a much more intelligent idea of the source of the rhythmical action of muscles. If we assume that the automatic production of stimuli in the cells of cardiac muscle depends upon a dissociation into definite ions, then there is no longer any uncertainty about Engelmann's theory of the periodic formation of stimulus-matter and its destruction with the systole.

The whole cycle of events would rank among those physico-chemical processes that are being revealed to us more and more. It is conceivable that the rhythm of stimulus-production may be altered by various circumstances primarily and independently of the excitability of the muscle. It is to be hoped that it will be possible, in the very near future, to give a final decision on this matter.

§ 6. **Stimulus-Conduction.**—In order to understand the action of the heart properly, it is necessary to know not only how and where the contraction-stimulus is formed at each systole, but also how it spreads from the *venæ cavæ* over the other portions of the heart, and what are the channels along which it is transmitted; for the progress of the wave of contraction must be effected by the successive stimulation of the muscle cells in the various chambers.

The power of transmitting stimuli is primarily ascribed to nerve fibres, and therefore it cannot be surprising that the conduction of the motor stimulus in the heart was referred to nerve elements, and particularly to the intra-cardial nervous system. And it was thought that either some reflex mechanism was here at work, as *e.g.* in the act of swallowing, or that more direct nerve fibres served to conduct the stimulus. In more recent times, however, the theory has found general acceptance that this power of conducting stimuli is inherent in the cells of cardiac muscle; the stimulus passes from cell to cell without the intervention of any nerve elements. The arguments in proof of this theory are continually multiplying, and of these the principal are as follows:—

It is generally held that the stimulus in non-striped muscle is really transmitted from cell to cell; and no fundamental objection can be raised against the view that a similar process is at work in the cardiac muscle cells which are in so many ways like those of the non-striped variety. Moreover, the microscopic examination of the musculature of the heart goes to show more and more clearly, that from the structure of the heart it is not only possible, but indeed very probable, that the transmission of stimuli in it takes place from cell to cell. In contrast with the cells of voluntary muscles there is no distinct line of division between those of the heart: there is no sarcolemma, the individual cells are united to one another by means of anastomoses; indeed the question has been raised whether it is possible at all to separate the individual cells. It follows from the most recent researches of Godlewski<sup>(36)</sup>

that even from an embryological point of view the muscular fibres of the heart are much more akin to non-striped fibres than to those of voluntary muscle: the cardiac muscle is said to represent originally a syncytium or one unified cell mass. The opportunity afforded by such a tissue for the conduction of stimuli is certainly no less than in non-striped muscle, where the cells, as we know, are united to one another by very fine protoplasmic processes.<sup>1</sup>

If we assume that the stimulus itself arises in the muscle cells, it is natural to refer the conduction of it also to the same source rather than to suppose that it is propagated outside these cells along nerve fibres.

But the investigations of Engelmann on the conductivity of the heart in 1894<sup>(18)</sup> had made this hypothesis very highly probable. It is possible by artificial stimulation to make the wave of contraction start from any point in the wall of the organ; the conduction therefore takes place within the wall in all directions. Thus it is quite easy to make the heart contract in a direction opposite to the normal. If we assume that the stimulus is conducted by the muscle this phenomenon is quite intelligible, while on the hypothesis of the action of a nervous-reflex mechanism it would be necessary to imagine that this reflex could be reversed, a condition that is surely inconceivable.

When a portion of the heart, *e.g.* the ventricle, is cut in such a way as to form a zigzag-shaped strip of muscle, this strip, in which the muscle cells are still connected with one another although there can hardly be any nerve fibres left uncut, conducts the stimulus just as well as a straight band of muscle would. This fact is a strong argument against the possibility of the stimulus being conducted by means of the cardiac nerves. Another argument against it is found in the comparatively slow rate of conduction in heart muscle; in the case of the frog it is, according to Engelmann, 300 times slower than in motor nerves. This rate is much less still at the junctions of the various chambers where they are united by very narrow bundles of muscle fibres. Engelmann was able to produce a similar delay by cutting a portion of the heart wall into two in such a way that the two parts still remained connected by a

<sup>1</sup> H. Eppinger (*Die toxische Myolyse des Herzens bei Diphtheritis, Deutsche medizinische Wochenschrift*, 1903, p. 257) says that the so-called cement-lines are always pathological; the musculature of the heart should therefore not only be developed from a syncytium but should remain as such.

narrow bridge of muscle; this thin bridge conducted the stimulus at a distinctly slower rate.

During systole the conductivity is temporarily destroyed, but it returns gradually again after each contraction. This fact affords an additional proof of the theory that those particles with which this function is connected, are also located in the muscle cells themselves and not in nerve fibres lying outside them. One would fain assume that a process is at work here similar to that which could be assumed in the production of the stimulus, viz., a dissociation into ions that have an effect on the conduction, which would be destroyed by the systole and necessarily restored again after it. In a recent paper, Göthlin<sup>(37)</sup> has made an attempt to trace the conduction of the stimulus in a living frog's heart, as well as the movement itself, to the action of certain ions. To go more fully into the discussion of this explanation, which involves a study of physical chemistry, would take us too far, and, moreover, the subject has hardly yet received sufficient proof to warrant it. But that we may possibly find the explanation of these various processes in the heart in this direction is most plainly indicated by the interesting researches of Loeb, Göthlin, and others (*cf.* Biedermann in *Ergebnisse der Physiologie*). Further details of stimulus-conduction in the heart will be fully dealt with again as well as in the chapter on the disturbances of stimulus-conduction.

§ 7. **Mutual Independence of the Various Properties of Cardiac Muscle.**—From what has been said it follows that the cells of cardiac muscle possess not only the properties of *excitability* and *contractility* which they have in common with voluntary muscles, but also those of *stimulus-production* and *stimulus-conduction*. The part which these various properties take in the action of the heart and their relation to each other form an extremely difficult, but very interesting, chapter in the physiology of the heart, and cannot but be regarded as highly important for an insight into the pathological disturbances of the cardiac functions. From the large number of facts that have been discovered about these properties of cardiac muscle it seems possible that a fuller knowledge of these pathological changes shall yet be obtained.

For further investigation into these functions it is of the highest importance to know that they are all independent of one another, so that it may happen that one property may even be absent altogether while another is present and greatly increased.

The study of the physiology of the cell during the past year tends to make it more and more probable that these functions are associated with atoms different in their composition and separate from each other in space, as Engelmann had declared long before. And recently <sup>(28)</sup> Engelmann has fully demonstrated that excitability (*Anspruchsfähigkeit*) and the capacity for work (*Leistungsfähigkeit*) are certainly different from one another. The stimulus and the power to respond to stimulation (*Reizbarkeit*) must also be separated as two totally different things; and he has shown from numerous examples that in the capacity for work the contractility which performs the work is in its nature quite distinct from the excitability on the one hand and from the conductivity on the other.

While investigating the duration of the refractory phase by means of the method of extra-systole, Engelmann was struck with the fact that the contractility and conductivity are not restored at the same rate after each systole. He demonstrated that the heart may completely lose its contractility and yet retain its conductivity by saturating a portion of the wall with distilled water, when he completely abolished the contractility in that part, while the conductivity remained unchanged.

From further experiments it follows that these functions, to quote Engelmann's own words, <sup>(28)</sup> "have a certain mean action under normal conditions of life, *e.g.* temperature, metabolism, mechanical variations, nervous influences, &c., and change in the same direction, with variations in these normal conditions;" but yet, under certain circumstances, "they may also vary independently of each other, and even in an opposite manner at the same time. This fact is theoretically of much greater importance than that of their simultaneous activity or usual variation in the same direction, for it proves that the latter relationship need not necessarily exist, and therefore the three properties of stimulation, conduction, and contraction do not make up one single function, but represent processes distinct from each other in space and time." He then goes on to compare the organs that are capable of stimulation to musical instruments, "of which there are some which are easy to make sound, but even with the greatest efforts give only a weak note, others that are difficult to play and yet emit a loud sound, while there are others again easy to play and possessing con-

B

siderable volume of sound, or, on the other hand, difficult to sound and giving out a very weak note."

Now, the heart is, as one would have expected, so constituted that it may not only be compared to one class of these instruments, but under the influence of the nervous system it is sometimes like one class, sometimes another, according to the requirements of the moment. In inquiring into the action of the nerves on the heart, therefore, the necessity for this mutual independence of its functions is again made apparent.

§ 8. **The Action of the Nerves on the Heart.**—Although it was formerly thought that the cardiac nerves modified the action of the heart by exercising an influence on the regulating intra-cardial nervous system, we now know that they influence the cells of the heart directly, by changing in the most diverse manner its fundamental functions. Instead of the simple quickening and slowing of the heart-beat, which are quite unable to explain fully the many different changes in its action, we now know that the nerves have an effect upon all the four properties in a positive as well as negative sense. When we reflect that these changes in function may occur in the most varied combinations, that the systole at the same time reacts on these properties, and that the alteration of one function has usually a secondary effect on another, we can see that an extremely complicated action on the part of all these various factors has to be explained, and that a vast field is open for research. And yet the following review may show that a great deal has already been established. We can only deal with the main facts here, but in the chapter on the pathological changes through nerve influence, this subject will be taken up more fully. The methods and the results attained with them can be best found in Engelmann's most recent papers <sup>(24 29)</sup> in which a full bibliography is also given.

Influences that affect the production of the motor stimulus are called (after Engelmann) *chronotropic*. *Positive chronotropic influences* are those which accelerate the stimulus-production, shorten the period of stimulation, and therefore increase the rate of the beats; *negative chronotropic influences* are such as have the opposite effect. These influences are primary when they affect the stimulus-production directly; they are called secondary, when in consequence of a change in the conductivity or the excitability, the result of the stimulus-production, i.e. the

rate of contraction, is altered. The conductivity can be similarly affected in a positive and a negative direction, up to complete abolition. In this case we speak of *dromotropic* influences; and this change in function under the action of the nerves may be either *primary* or *secondary*. Thus by increasing the number of beats the conductivity undergoes a secondary negative change.

Influences that affect the excitability are spoken of as *bathmotropic*; and we use the term *positive bathmotropic* influences when the excitability, which is measured by the lowest stimulus that produces a contraction, is raised.

Finally, there are influences capable of changing the most manifest of all the functions of the heart, viz., the contractility, in a positive or negative sense: they are called *inotropic*. What has been said about the primary and secondary chronotropic and dromotropic influences applies also to the bathmotropic and inotropic.

It is at once apparent how difficult it may be to separate these various influences in any concrete case. Take, for example, the simple case of the standstill of the heart from vagus stimulation. This condition, then, may result from a cessation of the stimulus (*i.e.* through a primary negative chronotropic influence), or from the diminution of the excitability which causes the stimulus present to have no effect (*i.e.* through a primary bathmotropic influence). But it may also be due to the fact that the stimulus is not conducted onwards, and hence the heart remains in diastole. Moreover, the stimulus, excitability, and conductivity may all be unchanged and yet the heart remains at rest through the paralysing effect of a negative inotropic influence on the contractility. And as a matter of fact it is not merely with these four possibilities that one has to reckon; for in stimulation of the vagus there are the most varied modifications of every single nerve influence and the most varied combinations of all these influences. Any one that follows the more recent researches of Engelmann and his disciples will understand how extraordinarily difficult the analysis of these changes in the functions of the heart is, but he will at the same time find that more and more progress is being made to bring this analysis to a successful result. Two important conclusions can be drawn from these analyses: (1) That the fundamental properties of the cardiac muscle cells are within wide limits really independent of one another; and (2) That for

the further extension of our knowledge of the heart's action and the pathological changes of these functions, it is absolutely necessary to regard them as quite separate and distinct in their character.

**§ 9. Objections to the Theory of the Mutual Independence of the Cardiac Functions.**—The facts that have been brought to light by the study of the influences of the nerves on the heart provide material to enable us to give a final refutation to the views of two observers, who, while accepting the "myogenic" theory, have endeavoured to give a more simple explanation of the nature of the heart's action.

Muskens found, from his exhaustive researches on the action of the vagus of the heart, <sup>(81)</sup> that the influences of this nerve on the stimulus-conduction play an exceedingly important part in the various irregularities of the heart. He formulated the theory based on these observations that the dromotropic influences exclusively control the heart's action, and, therefore, the chronotropic, bathmotropic, and inotropic cannot come primarily into play, but only secondarily through a diminution in the conductivity. A negative inotropic effect, he thinks, must then be inferred from the fact that through the partial blocking of the conduction a portion of the muscle cells is unable to contract, and hence the contraction is weaker. In this way he thought it also possible to explain Bowditch's staircase phenomenon.

It will probably appear at once unfair to assume that the conductivity is the only property of the heart that can vary primarily, while the other three, stimulus-production, excitability, and contractility, should not. But direct proof against this hypothesis has been adduced by Engelmann, <sup>(24 25 26)</sup> who showed conclusively that inotropic and chronotropic influences occur very frequently primarily and absolutely independently of dromotropic, *e.g.* in one and the same portion of heart-muscle a strong negative inotropic effect may occur while the conductivity remains the same, or is even increased. It is certainly true that dromotropic influences may have a considerable secondary effect on the other functions, but, while it would make the matter more simple to say that the former are the sole results of vagus stimulation, it would not be in accordance with fact.

H. E. Hering <sup>(41)</sup> has expressed the opinion that the independence of the various cardiac functions has not been proved yet, and

thinks that stimulus-conduction, excitability, and contractility, which always vary in the same direction under "natural" circumstances, cannot be regarded as separate entities, but must rather be taken together under the term "stimulability" (*Reaktionsfähigkeit*). Engelmann has refuted this view in his most recent works, and proved most conclusively the independence of the various functions by means of influencing the heart through reflex channels, *i.e.* under strictly "natural" conditions. The passage from Engelmann, quoted in § 7, is directed against Hering's theory, and he says further <sup>(3)</sup>:—

"If any one wishes to use the word 'stimulability' to denote the entire capacity of an excitable organ to respond to a stimulus, as H. E. Hering does, it is a quite permissible and convenient term, so long as he intends it to be merely a *short expression* for an intricate complex of physiological processes, without thinking of the various processes of which this complex is composed. But when it comes to the *investigation* into the causes of this stimulability, one is always compelled to split up the complicated process into its individual parts and to separate each physiological component part as far as possible. This is as true of the stimulability of a single muscle-fibre as it is of that of any organ or any highly developed organism. I could, therefore, only regard H. E. Hering's proposal to combine excitability, contractility, and conductivity under the expression 'stimulability,' and, therefore, to regard all the three functions as one, as a step backwards whenever this idea is intended to be more than merely a name, commendable only from its shortness for a very complex process."<sup>1</sup>

Hering's theory has been dealt with here at some detail, not because of the weightiness of his arguments, but because, with his conception of the mutual independence of the various cardiac functions, he must naturally deny the possibility of any pathological change in each function. In fact, on the basis of this view, he has declared my explanation of the irregularities of the heart, which I analysed and attributed to the disturbance of special functions, to be simply impossible. In discussing these irregularities we shall have to refer again and again to the untenable position which Hering dogmatically takes up.

It is then absolutely necessary for further physiological research; as well as for the analysis of pathological changes, to regard the

<sup>1</sup> Cf. Engelmann, 29.

functions of the heart as mutually independent. It would of course be easier for clinical work if one had not to bother oneself with all these physiological details, and it is therefore not surprising that Hering's view has been taken up by clinicians. Thus F. Kraus <sup>(64)</sup> expressed the opinion in a speech which he recently delivered at the opening of the second medical clinic in Berlin, that my attempts at a clinical analysis of the irregular pulse "do not appear to be quite successful," and said further:—

"The theory of H. E. Hering, according to which the changes in the excitability, contractility, and conductivity of the same muscle fibres in one part of the heart under natural pathological conditions occur as a rule in the same direction, furnishes us, I think, with a more simple key to the problem."

After the detailed account which has been given, one can only say that the simplicity of the key is not of such importance as what can be opened with it, and that if any one is really willing to take up the analysis, he will be compelled to investigate the heart's action in all its details, and not merely resort to collective terms.

§ 10. **Objections to the Myogenic Theory.**—The passion and the controversy that at first arose over this theory of the heart's action have now almost completely died away. But there are still two bitter opponents left, viz. Kronecker and von Cyon, two scientists of the highest repute, who have lately raised their voices against the theory of Engelmann.

Kronecker <sup>(66)</sup> opposes the "myogenic" theory in the paper, which he read at Hamburg, for various reasons, and amongst others that of the complete separation of the musculature of the auricle from that of the ventricle: a muscle-bridge, however, has been conclusively proved to exist by numerous investigators, and again recently by W. Ewald, <sup>(30)</sup> who instituted a fresh research into the conduction of stimuli between auricle and ventricle. Moreover, "Kronecker's puncture" into the upper third of the ventricular septum of a dog's heart is continually being trotted out as a proof against the "myogenic" theory. But the fact that this phenomenon has never yet been fully explained gives no more proof for the "neurogenic" theory than it does against the "myogenic," and after the latest explanation, which Kronecker himself gives (*loc. cit.*, p. 55) of it, that there is here a nerve centre, the stimulation (and injury?) of which makes the coronary arteries contract and therefore produces anæmia of the wall of the heart,

it is now beyond all comprehension to understand what significance this puncture still possesses as proof against the myogenic theory.

But Kronecker makes things much worse when he says further on: "The theory of nerve influences on the heart is required in pharmacology and clinical medicine." Has any advocate of the "myogenic" theory ever denied the influence of the nervous system on the heart? Has not Engelmann himself said, that with the multitude of nervous influences one might be inclined to ask whether the nerve elements present in the heart really suffice to explain these influences, rather than to inquire what purpose these nerves really serve? It is extraordinary to see this meaningless objection brought forward again and again. And the statement which was made at the meeting, although not printed in the Proceedings, was equally as bad, that it is quite impossible for the sake of a new theory to condemn the whole stock of pharmacological facts that have been collected for ages as worthless. Is not the truth the first consideration in scientific questions and in all practice founded on them? And has the pharmacology that was based on the older theories really rendered so much valuable service that a new theory on which to found more exhaustive investigation must be regarded as superfluous or not admissible? I would venture to say that it has not, and to alter the sentence of Kronecker, quoted above, so as to run: "Pharmacology and clinical medicine most urgently require a revision of the theory of cardiac poisons from the very beginning."

What has been said of Kronecker's paper may be repeated against von Cyon's latest work, <sup>(15)</sup> *Myogen oder Neurogen*. But von Cyon makes matters more easy for the advocate of the "myogenic" theory. It is only necessary to read his article in order to be convinced, that a question which has to be defended in this manner must be in a bad way; von Cyon has misunderstood the whole meaning of the myogenic theory, and we cannot but agree with Engelmann, <sup>(27)</sup> when he declares that it is not "to the advantage of either the subject-matter or its author" to reply at any length to this article.<sup>1</sup> A lengthy reply can therefore be dispensed with here also; as we said before, it is quite sufficient to read von Cyon's paper. It is, however, interesting from the clinical standpoint to observe that von Cyon adheres to the opinion that the "myogenic" theory has led clinicians astray, and threatens to confuse our view

<sup>1</sup> Cf. O. Langendorff in *Ergebnisse der Physiologie*, I., p. 345.

of the pathological changes of the heart. But here he shows that he is perfectly ignorant of the immense progress which has been made in the pathology of the heart through our knowledge of the significance of the cardiac muscle, and he may therefore be denied the right to express an opinion on the matter.

§ 11. **Importance of the Myogenic Theory in the Physiology and Pathology of the Heart.**—The myogenic theory has continued to hold its ground, and to advance towards complete evolution through the earnest researches of numerous workers. We owe it to this theory that we already know more about the various factors in the action of the heart than we do of any other organ. It is true that we possess extremely favourable facilities for investigating the action of the living heart, and that it is more easy to make direct observations and measurements of the effect of its action, its contraction, than is the case with many other organs. Nevertheless, the study of the cardiac functions can serve as an encouraging example for similar study of other organs; for the new theory has brought to light facts of the utmost importance not only for the heart itself but also for general physiology.

The fact that the chief functions of the muscle cells are independent in nature, and can also vary in magnitude reciprocally, throws a bright light on the various functions which are peculiar to the cells of so many other organs. Take, for example, the numerous functions possessed by glandular cells, which can not only produce a frequently very complex secretion, but may also be capable of giving off a special internal secretion. The wonderful experiments of Pawlow and his pupils have showed us to what a remarkable degree the composition of the saliva, the gastric, and the pancreatic juice may vary, and how this composition is suitable for every kind of food. And there can be no doubt that in this case also, each of the cell functions can be changed independently of the others, both by direct and indirect influences.

At first it aroused great surprise when it was stated, that the heart is to a certain extent an independently active organ; yet facts are being accumulated which point to the more or less independent action of other organs. And various facts go to show that the nervous system, this *deus ex machina* for everything that is not yet explained, is not the only factor capable of bringing about the connections between even distant organs and their co-operation; e.g. the internal secretion of many organs, and the influences of the

thyroid glands, the sexual glands, and other organs on the whole organism, as has been so clearly demonstrated, influences which are much more of a chemical than a nervous character. In this connection special interest attaches to the remarkable discovery of Bayliss and Starling,<sup>(8)</sup> that in the presence of an acid in the mucous membrane of the small intestine a substance, secretin, is formed, which chemically stimulates the pancreatic cells to secretion directly, and without the intervention of the nervous system.

Thus the facts that have been discovered in the investigation of the heart's action agree with general physiological principles, and have an importance for the physiology of other organs. But they are naturally of the greatest importance for the heart itself, and are much more able to unveil the mysteries of this ever active organ than the method of measuring the force of the blood through the heart which was formerly exclusively employed. By the latter method only the resultant of various factors working simultaneously is always measured, while the factors themselves remain unknown; and it must not be forgotten that in almost all cases only the action of the ventricle can be studied by this method. It teaches us ~~nothing~~ about the events occurring at the venous ostia which are of fundamental importance for the origin of the heart's action.

Thus, with the help of the new theory, we have found the heart to be a primarily self-acting organ, which, by virtue of its inherent properties, is able to preserve its rhythmical action even in the presence of many disturbing influences, and to meet many different claims on it. The fact that the automatic stimulus-production occurs with greatest intensity at the mouths of the great veins, and hence that the contractions always proceed from this spot, ensures that the blood-stream is propelled in the proper direction. The refractory phase guards the heart, both during and for a short time after the systole, from abnormal stimuli; and besides this advantage, this arrangement gives the heart an interval after each systole for the muscle to recover itself—it renders a condition of tonic spasm from continuous stimulation impossible, and ensures the due filling of the heart after every contraction. The fact that the contraction is always a maximal one gives the heart this advantage: (1) that it is thereby independent of the intensity of the stimulus; and (2) while weak but still effective stimuli produce the full effect, too strong stimuli are, *ceteris paribus*, unable to set up excessive action of the heart.

The function of stimulus-conduction plays an extremely important part in the automatic regulation of the heart. It is more advantage to the heart that the whole of its musculature transmits the stimuli than if the conduction, and therefore the due propagation of the contraction, were effected through a few nerve fibres; for considerable organic disease may have occurred in the heart, and yet conduction will be possible as long as there are still muscle cells connected to one another, as was shown by the experiment with the zigzag strip of muscle. It is an advantage that the conductivity is abolished or reduced after the systole, because by this means abnormal stimuli, which would be strong enough to excite a contraction as the excitability of the heart returns, perhaps cannot be conducted, and therefore cannot affect the whole organ. It will be shown afterwards, in treating of the pathological disturbances, how in irregular action of the heart, blocking of the stimulus-conduction is able to protect it from exhaustion when it is being stimulated too quickly by preventing the conduction of numerous stimuli, and thus guarding the heart from injury.

How far the peculiar action of the conductivity is capable of making possible a "myogenic self-regulation" of the heart has been most clearly demonstrated by Engelmann <sup>(21)</sup>. He found that, when extra-systoles are set off at the venous ostia on artificial stimulation at that point, the auricle and ventricle frequently exhibit a much smaller disturbance in their rhythm; and on closer analysis of this phenomenon it is found that the action of the ventricle is regulated more or less according to a definite rule. This is easily made clear by the help of Engelmann's diagrams (<sup>21</sup> Fig. I., III., IV.; cf. Fig. II., p. 27). The three abscissæ correspond to the time; the points in these abscissæ that lie in the same perpendicular plane represent the same moments of time. On the three abscissæ *S*, *A*, and *V* the systoles of the sinus, auricle, and ventricle respectively are marked by perpendicular lines; and the height of these ordinates corresponds to the size of the contraction. The lower ends of these lines represent the commencement of the systole. The dotted line denotes the conduction of the stimulus from sinus through auricle to ventricle. The length of the spontaneous periods is 10 units of time.

In Fig. II. *A*, an extra-systole is produced at 3 by an artificial stimulus. It strikes the sinus after 4 time-units. The systole is a small one, because the contractility has not yet returned to its full

strength; and the stimulus, coming so soon after the preceding systole, is not yet conducted so quickly, and therefore does not arrive at the auricle until 7 time-units after  $A_2$ , or at the ventricle until 8 units after  $V_2$ . The next spontaneous stimulus after it is conducted again nearer the normal. As the result shows, the rhythm in the sinus was 10, 4, 10, 10, &c., in the auricle 10, 7, 8, 9, 10, 10, &c., but in the ventricle 10, 8, 8, 8.5, 9.5, 10, &c., in which therefore the disturbance was least accentuated.

Other examples of the same phenomenon are given in Fig. II. B and C. In B we see that  $S_3$ , which came very quickly after  $S_2$ ,

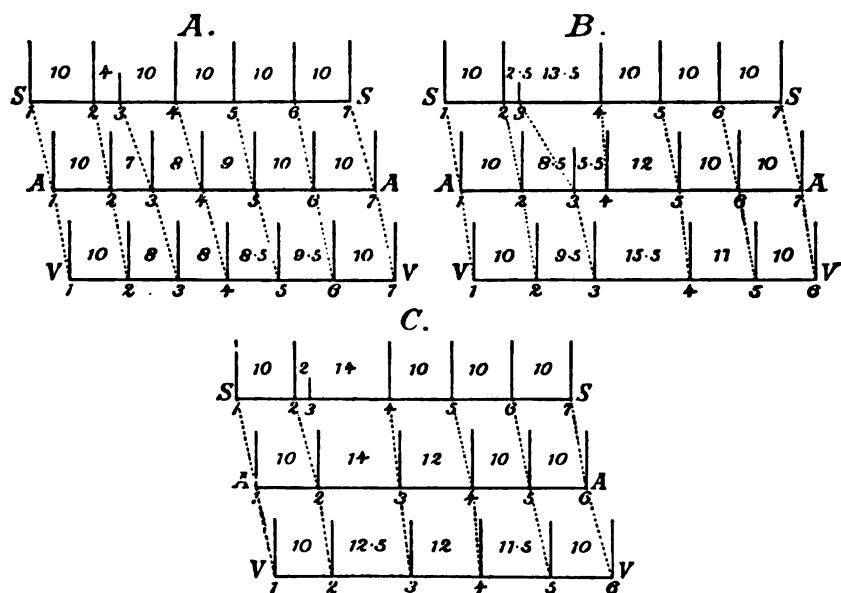


FIG. II.—After Engelmann.

is conducted to  $A$  very slowly; but as the conductivity has had time to recover itself again,  $V_3$  follows soon after  $A_3$ . On the other hand,  $S_4$  can be quickly conducted to  $A$ ; but as it now finds the ventricle still in the refractory phase, the latter does not contract at all. In  $C$  the extra-stimulus occurs still earlier; the sinus contracts, but as the stimulus is not yet conducted further, neither the auricle nor the ventricle contracts. After the long pause which thus ensues, however, the stimulus is conducted so quickly through the heart-muscle that  $A_3$  and  $V_3$  appear a little earlier than they would have done had the rhythm remained constant. In this way the disturbance is here again more equalised.

These examples, which were taken from actual cases, show most conclusively how the automatic heart, in virtue of its peculiar properties, is able without the intervention of the nervous system to preserve the rhythm of the ventricle, which is so absolutely necessary for the circulation, even in the presence of disturbing influences.

As regards the action of the nerves on the heart, it is at once clear that it is an advantage for the adaptation to certain requirements of the whole organism, that the various functions of the heart can each by itself be altered in a certain manner. We saw already that where the heart is irregular from over-stimulation, or there is excessive excitability, both negative bathmotropic and negative dromotropic influences are able to control its action; when the stimulus threatens to become too weak, a positive bathmotropic influence is still able to keep the heart's action intact. It is hardly necessary to emphasise the fact now, that our knowledge of the mutual variation of the individual functions under the influence of the nerves is therefore also of the highest importance for an insight into pathological disturbances.

Armed with the knowledge which this new theory of the myogenic action of the heart has gained for us, it is now an urgent, but obviously highly grateful, duty not only to bring the pathology of the heart into line with modern views, but also to submit pharmacology, and with it the whole chapter of cardiac drugs and therapeutics, to a thorough revision. How far the arrhythmia of the heart, which up to a few years ago was a perfect mystery to us, can help us to understand disturbances in its function will be shown more fully in the following chapters.

## CHAPTER II

### PHYSIOLOGICAL TYPES OF ARHYTHMIA

#### THE EXTRA-SYSTOLE

§ 12. **The Extra-systole in Literature.**—In recent years the opinion has gained ground in clinical circles that the extra-systole of the heart, which can be so easily produced and studied in experiment, can also occur spontaneously in man, and is the cause of irregularities of the heart and pulse that have long been recognised. In 1898 I <sup>(118)</sup> was able to prove that in the great majority of cases the so-called “early, premature, or abortive” contractions of the heart are extra-systoles, similar to those that are now known in physiology. Almost at the same time, and independently of me, Cushny <sup>(13 14)</sup> discovered the same fact. Henschen <sup>(39)</sup> showed in his work on this subject that he was also on the right track. About the same time Langendorff <sup>(67)</sup> made the suggestion that the spontaneous premature contractions seen both in man and in the lower animals were extra-systoles, but was not in a position to study the matter in man.<sup>1</sup> Finally, H. E. Hering <sup>(40)</sup> demonstrated the fact again in 1900, and proved it by experiment.

The occurrence of spontaneous extra-systoles in man not infrequently gives very valuable information about the disturbances of the functions of the heart, which are the cause of its arrhythmic action, in the same way as their production in experiment helped in the study of the behaviour of these functions in the various phases of the cardiac cycle.

§ 13. **The Extra-systole in the Frog's Heart.**—In § 4 we saw how extra-systoles can be produced by electrical stimulation of the sinus, auricle, or ventricle of the frog's heart, and that these extra-contractions are smaller or greater according as the part was stimulated earlier or later in the diastole. The result of these extra-systoles is to make the auricle and ventricle refrac-

<sup>1</sup> In consequence of a remark made by Langendorff (I., p. 296) I should like to state here that my paper, which was written in Dutch, appeared in August 1898, and in April of the same year I delivered a paper on this subject before the Medical Society of Utrecht.

tory to the next spontaneous stimulus that arises, and therefore a beat is missed, and it is not till the next succeeding stimulus, which, moreover, occurs exactly at the moment at which it would have occurred had there been no extra-stimulation, that a contraction is again produced. Hence arises the compensatory pause of the heart, which follows every extra-systole, as is shown in Fig. I. When, however, the venous ostia are stimulated, the extra-systole is not followed by a compensatory pause, a phenomenon which proved the fact that the physiological stimulus is not rhythmically conducted to this point, but arises periodically there.

§ 14. **The Extra-systole in the Mammalian and the Human Heart.**—Before it was possible to apply the laws that govern the frog's heart to the pathology of the heart in man, it was absolutely necessary to know whether the mammalian heart is subject to the same laws. It is, of course, probable that the function of the heart will be fundamentally the same in all vertebrates, but yet it was very desirable to obtain experimental proof of this fact. Cushny and Matthews <sup>(12)</sup> were the first to prove that the function of the mammalian heart is exactly the same as that of the frog. They experimented with the mammalian heart after Engelmann's method of extra-systole, and found that exactly the same laws of refractory phase and compensatory pause are at work in it as in the frog. There was only one point in which they observed a difference, viz. when the auricle is stimulated artificially, the compensatory pause following the extra-systole is not always completely compensatory, i.e. it is usually too short. Now and again it was of proper length, but more often it was considerably shorter than was to be expected, and sometimes it was almost entirely absent (<sup>12</sup> p. 224). "So long as the interval  $A_s-A_p$  is of considerable length the compensatory pause of the auricle is really compensatory, i.e. the interval between the last spontaneous contraction and the post-compensatory is equal to two auricular periods. When, however, the stimulus occurs earlier in the excitable phase, a true compensation does not occur, the post-compensatory systole appears too soon. . . . When  $A_s-A_p$  is short, the compensatory pause preceding the next spontaneous contraction is always incomplete."

In explanation of this difference they say: "Either the wave of contraction proceeds from the auricle to the great veins and there sets up a forced contraction which returns to the auricle and

causes the premature (post-compensatory) systole, or the excitability of the auricle goes on increasing until it explodes in a contraction that is independent of the great veins and arises in the wall of the auricle itself. Which of these two explanations is the correct one it is impossible to say, and we think it would be useless to compare their relative values until the movements of the great veins have been more closely studied."

I have previously <sup>(118)</sup> expressed the opinion that the auricle of the mammalian heart might possibly possess a greater power of producing stimuli automatically, for the reason that in the phylogenetic development a portion of the sinus venosus goes to form the auricle.

H. E. Hering <sup>(40)</sup> has also been able to confirm this peculiar behaviour of the auricle in the mammalian heart, which Cushny and Matthews described, and he says (p. 16): "The earlier the moment of stimulation occurs in the excitable phase of the auricle, the shorter is the artificial bigeminus (interval between the last spontaneous and the post-compensatory systole of Cushny and Matthews); and the later it occurs, the nearer does the time-value of the artificial bigeminus come to that of two normal cardiac cycles." And he found further, "That the earlier the moment of stimulation falls into the excitable phase, the longer is the compensatory pause. These results show that the law of the conservation of the rhythm of physiological stimuli certainly holds good for the auricle of the mammalian heart, though the relationship is not so simple as in the ventricle."

In a subsequent communication <sup>(42)</sup> Hering again drew special attention to the fact that the compensatory pause is not always incomplete after stimulation of the auricle.

It is remarkable that these physiological facts agree exactly with what Mackenzie <sup>(74)</sup> found in 1894 by careful analysis of the venous and liver pulse, viz., that when a "premature" systole starts from the auricle in man, it is more often followed by an incomplete compensatory pause.

I have recently endeavoured to show <sup>(124)</sup> that there is no fundamental distinction between the frog's heart and that of the mammalian in this shortening of the compensatory pause after stimulation of the auricle in the latter, and that an easy explanation can be given for this phenomenon as well as for the laws governing its occurrence as laid down by Cushny and Matthews and H. E.

Hering. I shall not enter into this explanation in detail here, but would refer the reader to the paper I have just alluded to; I will only observe that the question as to whether the compensatory pause will be shortened or complete depends on whether the wave of contraction set up by the extra-stimulus travels backwards and reaches the great veins before or after the moment at which the physiological stimulus becomes active at that point. If this wave of contraction arrives at the great veins before that moment, the stimulus-matter which is here present is destroyed, and it takes the time occupied by a spontaneous period before the physiological stimulus has again become strong enough to produce a contraction (*cf.* § 5); the compensatory pause will then be the shorter, the sooner the contraction-wave reaches the great veins before the moment of the spontaneous systole. If the stimulus is applied so late in the auricular diastole that the contraction-wave does *not* arrive at the great veins before the spontaneous stimulus becomes effective, the spontaneous contraction has already begun at that point, and the artificial stimulus finds the muscle there refractory. The physiological rhythm of the veins is therefore in this case undisturbed. The fact which Hering discovered, that the earlier the stimulation of the auricle was made during diastole the longer is the pause itself, is easily explained by the condition of the conductivity. And finally, the fact that the frog's heart does not exhibit a similar disturbance of the rhythm of the veins from extra-systole of the auricle is explained in this way, that in it there are more than one break in the musculature between the great veins and the auricle (between veins and sinus, and between sinus and auricle). The motor stimuli are conducted much more slowly at these junctions (*cf.* § 6); an artificial stimulus acting on the auricle of the frog's heart will therefore have much less chance of reaching the veins before the commencement of the spontaneous systoles than in the mammalian heart, where these breaks do not exist between the veins and the auricle (*cf.* <sup>124</sup>). It is, therefore, a difference in anatomical structure, and not a fundamental difference in the mechanism of these two types of hearts, that produces the difference in their behaviour after stimulation of the auricle. This fact lends further support to the view that the results obtained from the frog's heart can *mutatis mutandis* be applied to the mammalian, and therefore to that of man.

With the help of the physiological data which have been out-

lined here, it was an easy matter (as will be shown more fully in the next paragraph) to prove that in man the heart is frequently stimulated into extra-systoles. After this proof had been discovered by Cushny and myself, and later by Hering, this theory found acceptance in clinical circles. Lommel,<sup>(72)</sup> for example, has recently discussed the occurrence of extra-systoles in a very exhaustive paper. Mackenzie, who continued the work above mentioned<sup>(74)</sup> which he began in 1894, without going deeply into the physiological aspect of the question, has given us in his splendid book, "The Study of the Pulse,"<sup>(75)</sup> most valuable material for the analysis of irregularities of the heart, which shall be repeatedly made use of in this work.

With the help of the work that has already been done, and through further observations of my own, I shall explain in the following paragraphs the part which the extra-systole plays in arhythmia.

§ 15. **The Proof of Extra-systole in Man.**—The simplest case in which one can see the extra-systole in man is that of a pulse perfectly normal except that now and then a beat is missed, the so-called *intermittent* pulse. When one auscultates the heart while feeling the pulse, it strikes one at once that at the beginning of the intermission the heart gives apparently two beats in succession instead of one. What is then heard may be represented diagrammatically as follows:—

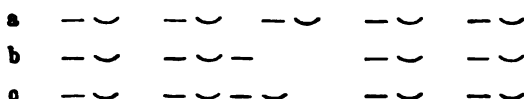


FIG. III.

If *a* represents the normal rhythm of the cardiac sounds, one hears during an intermission either a single sound (*b*) or two sounds (*c*) immediately after the preceding heart sounds; then follows a pause, after which the sounds return again into their normal rhythm. These peculiar sounds can hardly be explained in any other way than that they are due to a systole occurring at an unusual period. This systole, moreover, can be easily felt in the region of the cardiac impulse and can readily be recorded on a cardiograph. Finally, this systole frequently gives rise to a large or small pulse-wave in the radial artery, as will be shown more fully again.

It will appear to every one that has followed the above explanations highly probable that we have here to deal with an extra-

systole. But in order to prove this, it must be shown that a real compensatory pause occurs here; if it were not an extra-systole but simply an early occurring physiological, normal systole, it would be impossible to understand why the latter should not be followed by a normal, or an abnormally long or short, diastole.

But if we measure the length of the intermissions in the pulse tracing it is found that the intermission is exactly equal to twice the preceding periods; a whole pulse-beat has actually dropped out, there is a full compensation in time after the occurrence of the premature systole, and the physiological rhythm is not disturbed. But this proves that it was not a premature physiological systole

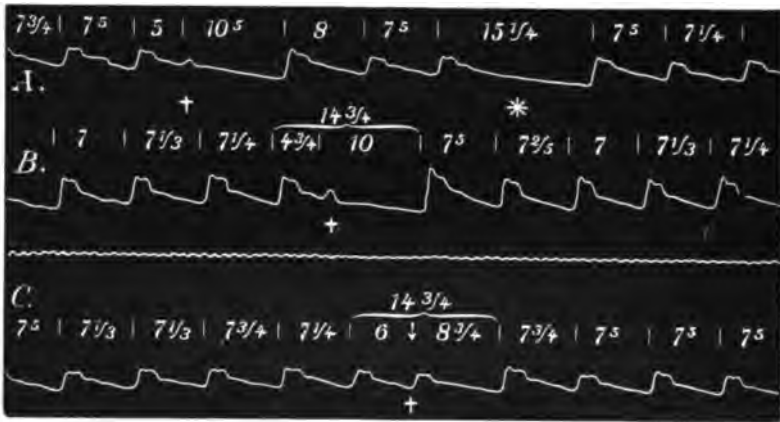


FIG. IV.

that occurred, but an extra-systole, such as is followed in experiment by a compensatory pause: and a physiological systole dropped out.

Fig. IV. illustrates this. This pulse-tracing was taken from a man eighty years of age, who was suffering from arterio-sclerosis, but showed an otherwise regular pulse. The numbers represent the length of the period in  $\frac{1}{16}$  seconds.<sup>1</sup> In *A* at \* we see a pure intermission, while at † in *A*, *B*, and *C*, a larger or smaller pulse-wave is visible in the intermission. The intermission, i.e. the interval between the normal beat that preceded the extra-systole and the post-compensatory systole, is exactly twice as long as the normal pulse periods, as is seen from the accompanying figures. The

<sup>1</sup> Even in those cases where the time-line has been omitted in the illustrations for the sake of convenience in reproduction, the numbers in all of them were obtained by means of such lines either in .1" or .04".

physiological rhythm of the heart, therefore, is continued over the irregularity.

These extra-systoles that occur in man correspond in the smallest details with those that are obtained experimentally.

In most cases the compensatory pause is a little too short, as in experiment: the post-compensatory systole appears a little too soon. Engelmann tries to explain this almost constant phenomenon by the undeniable fact that the circulation in the venous portion of the heart is for a short time seriously disturbed by the extra-systole, and that possibly as the result of this the automatic stimulus becomes effective a little sooner than when the rhythm is undisturbed. Besides, there is another factor, viz., that when the post-compensatory systole takes place, the heart-muscle has had a longer pause, and the stimulus is thus conducted more quickly through the heart; hence the contraction of the ventricle will occur more quickly after the moment of stimulation at the vena cava, and therefore will appear a very little earlier: the ventricular wall will also contract more quickly, and the pulse-wave will be transmitted more rapidly along the arteries, and will also show itself somewhat earlier in a tracing of the radial pulse.

The longer rest which the heart gets after the extra-systole also explains the fact that the "post-compensatory" systole, to which Bottazzi <sup>(7)</sup> and Langendorff <sup>(67)</sup> have given special study, is larger and fuller than the systoles occurring in the normal rhythm; after the pause the muscle has got more opportunity than ordinarily to regain its contractility. In the pulse-tracing in Fig. IV., as well as in most of the other tracings that are given in this book, a large pulse-wave after the pause corresponds to this large post-compensatory systole; possibly the fact that the ventricle is more filled with blood after the pause has something to do with this. In consequence of this large post-compensatory systole the next succeeding contraction, with its corresponding pulse-wave, is again somewhat smaller; this may be due to the greater exhaustion of the contractility by the preceding strong systole, but is often merely the result of an imperfect filling of the heart so shortly after the full post-compensatory systole. The second succeeding pulse-wave frequently appears smaller, merely because the artery was still fuller of blood after the large first post-compensatory beat; it therefore looks smaller, and yet it rises to the normal height in the sphygmogram. This greater filling of the artery (a

smaller fall in the line) is shown, *e.g.* in Fig. IV. to some extent, and much more markedly in Fig. V., *B*. According to Engelmann and Hering the first physiological period after the compensatory pause is frequently slightly prolonged. This phenomenon also occurs often in man; perhaps it is at times caused by the fact that the post-compensatory systole is performed, as we saw before, more rapidly than normally, and hence the post-compensatory pause appears a little too soon; when, therefore, the second wave is transmitted at the normal rate again, the distance between the two pulse-waves must be a little larger than the normal period (*cf.* the chapter on Disturbances of Conduction).

As we stated briefly already, the sphygmographic tracing of the intermission, which is frequently represented by a uniformly sinking

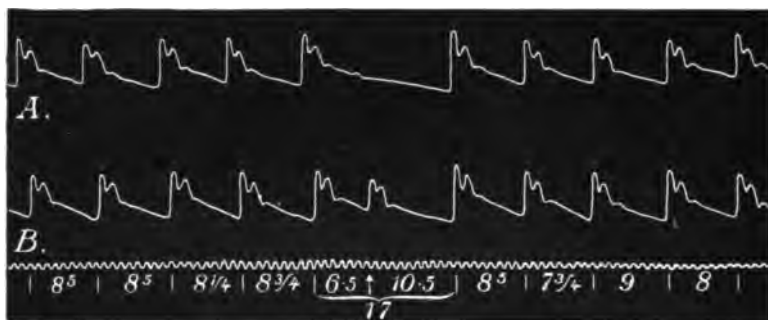


FIG. V.

line, exhibits in most cases an extra pulse-wave as the result of the extra-systole. A very good example of this is seen in Fig. V., taken from the same patient as Fig. IV., where an almost perfect intermission is seen in *A*, and in *B* a very distinct extra pulse-wave (see also Figs. IV. and VI.).

The occurrence of an extra-systole depends on three factors: the energy of the extra-ventricular systole, the volume of blood in the ventricle, and the blood-pressure in the aorta. These factors, again, depend on the moment at which the extra-systole occurs. In the beginning of the diastole, shortly after the preceding systole, the force of the extra-systole is still small, due to the imperfect recovery of the contractility of the muscle; very little blood will have yet run into the ventricle, while the pressure in the newly-filled aorta is then greatest. It will therefore hardly be possible for an extra-systole to overcome the pressure in the aorta, open the

semilunar valves, and transmit a wave into the periphery of the arterial system; the extra-systole will therefore produce only the first cardiac sound, while the second sound (the stretching of the semilunar valves) will not occur; thus we have the case illustrated in Fig. III. *b*. But, if the extra-systole appears later in the diastole, the case is different: the contractility of the ventricle is restored, its cavity is better filled with blood, and the pressure in the aorta is much less, and so the extra-systole opens the semilunar valves, forces a wave of blood into the aorta, thus producing the second cardiac sound (Fig. III. *c*), and is shown in the tracing as an extra pulse-wave. If the extra-systole occurs a little before the time at which the next normal systole would have appeared, the extra pulse-wave may become as large as normal and be distinctly perceptible in the radial artery. This gives, then, the impression that a pulse-beat occurs a little *too soon*. It is evident, therefore, that the familiar phenomenon of an early-occurring pulse-beat, called by most writers the *pulsus bigeminus*, can also be produced by extra-systoles. Whether an intermission or a premature beat is observed in the pulse depends on whether the extra-systole occurs sooner or later in the diastole. The experimental researches which Hürthle<sup>(50)</sup> made on the blood-pressure led him to give a similar explanation.

This theory is not only of theoretical but of practical value, as any pulse-tracing from a person suffering from extra-systoles will show. In Fig. IV., and better still in Fig. VI., taken from another man seventy-six years of age, the gradations from a real intermission to an apparently very slightly premature beat are depicted; and in all the other tracings reproduced here similar gradations can be seen.

We must here observe that the extra pulse-wave in the tracing sometimes occurs simultaneously, or interferes, with the dicrotic wave, and in consequence of this it appears considerably exaggerated or almost completely obliterated, or at any rate altered considerably. A splendid example of this complication is shown in Plate I., Fig. 1, which was taken from a young man with a serious heart lesion (mitral incompetence and adherent pericardium). The cardiogram with the unmistakable extra-systoles is here indispensable for the proper interpretation of the pulse-tracing. The pulse-wave 1, caused by the extra-systole 1, appears in the radial artery at the moment when the dicrotic wave is just beginning to sink, and hence for a short period prevents the pulse-line

from falling. The extra pulse-wave 3 occurs during the fall of the dirotic wave, to which it thereby gives a second peak. The wave 4 forms a transition between 1 and 3. In 2, 6, 7, 9, and 10, the extra waves occur at the same time as the small wave, which follows, *e.g.* after 4, and hence appear to rise a little too far.

§ 16. **Extra-systoles which proceed from the Auricle or the Venous Ostia.**—It follows from the physiological experiments that were referred to in § 4 and § 14 that in the mammalian heart an

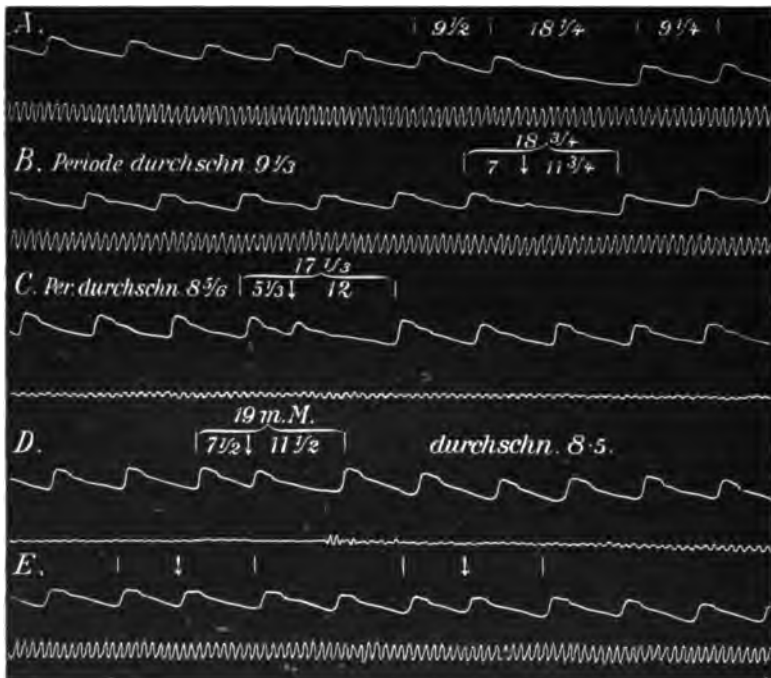


FIG. VI.

extra-systole that arises from the ventricle is invariably followed by a completely compensatory pause, while on stimulating the auricle the pause is frequently shortened. It was therefore natural to think that in those cases, where extra-systoles undoubtedly occurred and were followed by a too short pause, the extra-systoles possibly proceeded from the auricle, and not from the ventricle as is usually the case (see § 25). I have already in my first paper <sup>(18)</sup> on this subject endeavoured to explain such a case in this way. Cushny <sup>(13 14)</sup> has recorded some beautiful examples of this shortened pause, and has concluded that the

extra-systoles were "ventricular" or "auricular," according as the pause was fully or imperfectly compensatory. As we said before, we were unaware that Mackenzie <sup>(7)</sup> in 1894 distinguished between those two forms of extra-systoles, or, as he called them, "premature contractions." Nevertheless, H. E. Hering <sup>(8)</sup> did right in laying stress on the fact that extra-systoles with a short pause always arise from the auricle, while those that are followed by a complete pause may proceed from the auricle as well as the ventricle; and therefore the latter class cannot be put down straight away as being ventricular in origin.

In Fig. VII. this pause is regularly .1" or more too short; it is thus distinctly shorter than in the tracings of the other cases given in this book. In this case it is natural to suppose that

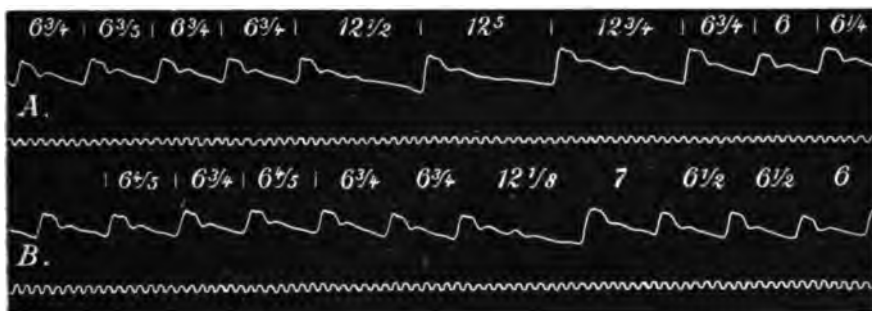


FIG. VII.

the extra-systoles arise in the auricle and not in the ventricle. This tracing was taken from a female with very marked mitral incompetence; in this lesion, however, the auricle is the first part to suffer; it is therefore very feasible to suppose that the auricle in this case is stimulated into extra-systoles. But the pause may be much shorter still in man. In Fig. 2 a (Plate I.) an extra-systole appears for a short period after every second normal beat, and each extra-systole is followed by a pause that is only a little longer than the normal. And in Fig. 3 (Plate I.), which, like the preceding, is of the greatest importance for other reasons, an extra-systole appears after every third normal beat. The length of the normal period (expressed in twenty-fifths of a second) is 24, while that of the pause following the extra-systole is 25.5-26. The compensatory pause therefore takes up at most 1.5-2 twenty-fifths of a second, and is thus by no means fully compensatory.

At the same time we must remember that these figures have only a relative value, because they were obtained at the radial pulse and not at the heart itself. We know from Engelmann's experiments that when an extra-systole arises at the venous ostia, there is no compensatory pause. It is therefore most probable that in the cases Figs. 2 and 3 (Plate I.) the abnormal stimulus arose very near to the venous ostia.

If now the stimulus actually began at the mouths of the great veins, there would necessarily be no pause, and we shall later on see cases in which this was probably what took place. Yet obvious difficulties at once confront any attempt to explain these cases. This question will be discussed more fully again (§ 24), but we must here remark that in man we are only able to diagnose the presence of extra-systoles by the more or less compensatory pause, and that, if the pause is absent altogether, we are usually not in a position to determine whether we have to deal with extra-systoles or early occurring physiological systoles.

Finally, we must bear in mind that extra-systoles proceeding from the mouths of the great veins need not always be repeated in the ventricle in the same uniform succession. We saw in § 11 how the automatic regulation of the heart destroys an extra-systole and produces an irregularity of the ventricular rhythm, for which it seems hardly possible to give a proper explanation.

§ 7. **The Nature of the Shortening of the Compensatory Pause.**  
—The usual length of the compensatory pause after an extra-systole may be altered from various causes. This ought to be remembered should the attempt be made to put down every case of a shortened pause to an *auricular* extra-systole. This cannot be done, as the following examples and others, which shall be given later, show.

The first example of this kind is found in those cases where the extra-systole occurs exactly at the moment when the excitability and contractility of the cardiac muscle have been partially restored, when the next physiological stimulus becomes effective, and therefore the corresponding physiological systole is not dropped. It is then naturally not followed by any compensatory pause. It is sometimes possible to interpolate an extra-systole in this manner experimentally when the heart is beating slowly, and even in man the same condition is observed in rare cases.

When one auscultates the heart in such cases one hears now

and then a dull sound during the pause between two beats (Fig. VIII. *a*). At other times, however, one hears two sounds interpolated (Fig. VIII. *b*), and then feels a small extra pulse-beat. An example of this latter condition is given in Fig. IX. On carefully measuring the time, the first small elevation is found to corre-

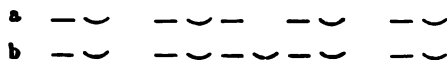


FIG. VIII.

spond to an extra-systole, but the second is produced by the next normal systole and not by a second extra-systole. A compensatory pause is out of the question. From a superficial examination of this case one might be inclined to think that two extra-systoles occurred. It is probable that Mackenzie<sup>(75)</sup> also observed an interpolated extra-systole of this kind in Fig. 83 of his book: in this case the second small pulse-wave would not be an extra-systole, but the next succeeding physiological systole slightly reduced in size; if the ascending limb of this contraction were prolonged downwards this explanation becomes a very feasible one.<sup>1</sup>

A very remarkable instance of regular shortening of the compensatory pause can be shown in Fig. 4 *a, b* (Plate I.). These pulse tracings were taken from a man dying in uræmic coma.

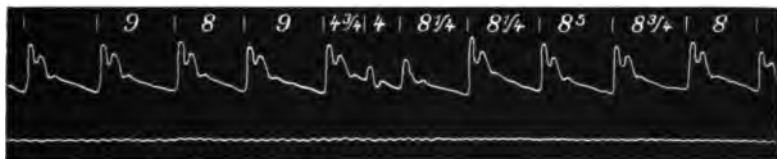


FIG. IX.

After the pulse had shown various irregularities, which are more fully analysed in § 33, and returned again for a short time to its regular quick rate with a period length of 14–15 twenty-fifths of a second (Fig. 4 *a*) it suddenly began to beat with half-frequency; only every second stimulus produced a systole (for the probable cause of this dropping out of every second systole see § 33). During this half-frequency now extra-systoles occurred again and again: and they were invariably followed by a considerable pause, but never by one so long as to be compensatory for the half-frequency. What took place in this heart is shown most plainly by Fig. 4 *b*. During the half-frequency the physiological stimulus

<sup>1</sup> Vide Appendix 1.

arose in the middle of the long pause, but the heart did not respond to it. The succession of regular stimuli to the heart may be marked by small arrows ↓. An extra-stimulus ↓ now arises in the ventricle. The result is an extra-systole which renders the next physiological stimulus ineffective. If now the physiological stimulation also followed with only half-frequency, the pause would have to last till the stimulus  $z$ , and would therefore be compensatory for the half-frequency. But the heart is stimulated at the old rate; and because it has already had a long rest up to  $y$ , the stimulus produces a contraction at  $y$ . The result is, as is proved on measuring the tracing, that the pause is shortened, but in a perfectly regular manner. The interval between the preceding and the post-compensatory physiological systole is not equal to twice the length of the period, but is exactly equal to one and a half periods. And this shortening of the compensatory pause was not only met with in this one example, but was observed in all the extra-systoles that occurred, without exception.

§ 18. **The Compensatory Pause in Irregular Action of the Heart.**—The regular behaviour of the compensatory pause and the continuance of the physiological rhythm are naturally to be expected only in cases where this rhythm is a regular one. When the physiological stimulation of the heart is irregular from some cause or other, we may at once expect that when an extra-systole occurs the length of the compensatory pause may vary very considerably. Examples of such irregularities are given in Fig. 2  $b$  (Plate I.), where in all probability a nervous influence is at work (see § 61), and the compensatory pause is altered along with the change in the rhythm of the stimulus. The occurrence of too long pauses (Fig. 35) may also be explained in the same way. It has hitherto been denied that too long pauses could occur; but that they do occur is shown by the figures above mentioned, as well as by others. But in this case other influences must be thought of, and particularly a nervous influence, which can be shown to be present in these cases (§ 61).

A very good example of irregularity of the heart is given in Fig. 5 (Plate II.). The upper tracing is the cardiogram; the lower is taken from the radial pulse. It is quite obvious, without measuring the time of the beats, that systoles and extra-systoles are occurring here without the slightest regularity, and that while the

pulse pauses are all apparently uniformly equal, an extra-systole is being recorded in the cardiogram at one time, while at another the heart remains quiescent. In § 25 this pulse will be discussed more fully, and the question will be raised whether we have any right to call these extra-systoles at all.

§ 19. **Groups of Extra-systoles.**—It is not at all uncommon in the human heart for several extra-systoles to appear in succession as the result of abnormal stimulation. In this way very complex irregularities may arise in the heart as well as in the pulse tracing, and yet in many cases are capable of a correct interpretation.

Two extra-systoles sometimes follow so quickly after each other that only one physiological beat is missed; in such a case, as in

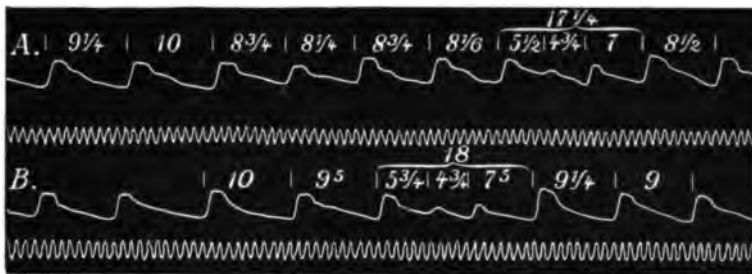


FIG. X.

Fig. X., two small elevations can be observed in the pulse tracing in one intermission. But if the second extra-systole occurs a little later, two normal beats may drop out, as in Fig. XI. The whole period in which the extra-systoles take place is then equal in length to three normal periods instead of two. Those authors that speak

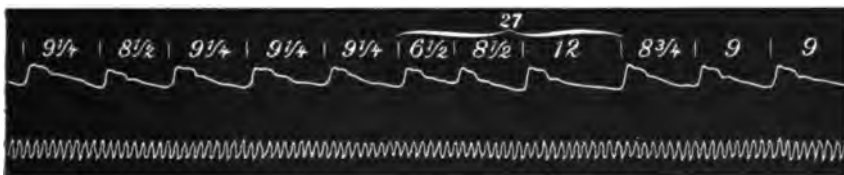


FIG. XI.

of *Pulsus bigeminus* when one extra-systole occurs call this form with two extra-systoles *Pulsus trigeminus* (cf. § 69).

The physiological rhythm in this case is undisturbed, and in the same way it may go on, even where there is a long succession of extra-systoles, as Cushny showed in some very good examples. <sup>(13 14)</sup>

But the venous rhythm does not always remain undisturbed. In Fig. 1 (Plate I.), a single extra-systole (extra-systole 3 and 4) is followed by an almost fully compensatory pause; but where several occur in succession the compensation is not complete, as the accompanying numbers show. In this instance it is possible that the extra-systoles, or at least some of them, arise from the auricle, and hence the compensatory pause appears shortened; but where there is a series of ventricular extra-systoles it is perhaps not impossible, especially when they occur very rapidly, that the contraction wave begins at the ventricle and travels back to the venous ostia, and there disturbs the rhythm in exactly the same way that the rhythm of the venous ostia can be overruled in experiment by frequent stimulation of the ventricle.

Examples of large groups of extra-systoles are given by Mackenzie <sup>(75)</sup> and others, and can also be found in some of the older authors. Similar examples are given here in Figs. 37-41 (Plate VII.). These cases, however, cannot be called extra-systoles without any further consideration, as will be shown in § 25, and in the last paragraphs of the book: it will be found that in many of them we must rather think of an increased frequency of the heart from chronotropic or bathmotropic influences.

§ 20. **Regular Extra-systoles.** A certain regularity in the occurrence of extra-systoles can not very infrequently be detected. When persons suffering from extra-systoles are observed for a considerable time, it is remarkable that there are periods with numerous extra-systoles that alternate with others without any. One then frequently knows that one extra-systole is followed by several more, and advantage can be taken of this in taking a pulse tracing.

But a definite regularity more frequently takes this form, that an extra-systole occurs after every normal beat, or every two, three, or more. In my first contribution to the subject of the extra-systole (<sup>118</sup> p. 193, Plate I., Figs. A and B), I gave instances and illustrations of such cases. I am now able to reproduce two better examples of this condition, which is, of course, often perceptible, but cannot always be equally well recorded. In Fig. 2 *a, b* (Plate I.), an extra-systole occurs for a considerable period after every two normal beats. In Fig. 6 the intermission that comes in after every second systole is also caused by an extra-systole, though the latter has not been recorded in the tracing. I have another case exactly similar

to Fig. 6 in my possession, In Fig. 3 (Plate I.) every third beat is followed by an extra-systole. In this way a regular irregularity, an *Allorhythmia*, may arise, which appears as a regularly intermittent pulse when, as in Fig. 6, the extra-systole does not produce any perceptible beat in the pulse. In these cases the length of the intermission is independent of that of the compensatory pause; it is thus equal to two periods, or is shorter as in Fig. 2 and Fig. 3.

When now every normal beat is followed by an extra-systole for some time, as not infrequently happens (*cf.* Fig. VII., where this occurs three times), a form of Bradycardia appears, viz., halving of the pulse frequency. Every case will, therefore, have to be examined as to whether each systole is followed by an extra-systole, or whether simply every second beat is missed, a condition which will be described more fully again.

Lommel <sup>(72)</sup> also speaks of the regular occurrence of extra-systoles in his valuable work (p. 35, &c.); and, as he remarks, one may readily suppose that there is here an interference between the normal and the pathological stimulation. Mackenzie <sup>(76)</sup> also gives a number of beautiful examples of regular extra-systoles.

§ 21. Does a real Bigeminal Action of the Heart exist?—We must here refer to a special form of this regular occurrence of extra-systoles which is of great importance for the explanation of pulse irregularities. It sometimes appears as if every systole is followed by an extra-systole for a very long time, for days and weeks, without a break. When this condition stops it is followed by a regular action of the heart: we find in such patients, therefore, either a second beat immediately after every systole, or regular movement of the heart. I was constrained to ask myself whether these were really extra-systoles, for when *they* appear one usually finds that it is exceptional for them to occur regularly, and even then at quite irregular intervals (*cf.* Plate I., Figs. 2 *a* and 26, which were taken from the same tracing, and the other cases here recorded, in which the regular intervals are exceptional).

If, however, we carefully analyse the contractions of the heart and the pulse periods in these cases, we find that the second beat bears a very peculiar relation to the first: the compensatory pause after the second beat is absent altogether. If these were extra-systoles, they must arise at the venous ostia, a conclusion which at once makes it very doubtful that they are of the nature of extra-systoles (*cf.* § 16). But it is absolutely proved that they are

not of such a nature, by the fact that these two systoles, which closely follow one another, are found to have a fixed relation to each other in time even when the rhythm is otherwise irregular, the second beat invariably following the first after a constant interval which does not vary more than .01". In this case we have no right to call the second beat an extra-systole; on the contrary, one must assume there is here a bigeminal action of the heart, a true "bigeminy," in contradistinction to the false bigeminy produced by extra-systoles. These remarks are illustrated by Figs. 8 *a*, 8 *b*, and 9 (Plate II.). This subject will be discussed more fully in the section on so-called *Pulsus bigeminus* (§ 68).

§ 22. **Influence of the Frequency on Extra-systoles.**—Extra-systoles usually occur in greater numbers when the heart is beating slowly than when it is acting quickly. This fact can easily be observed by examining the patient standing up (*i.e.* with more rapid pulse) and lying flat down; extra-systoles are nearly always much more numerous in the latter position than in the former. The explanation is easily obtained from our knowledge of physiology. With a slow pulse the excitable phase lasts much longer after each beat of the heart than with a frequent; the nearer the systoles approach each other, the nearer do the refractory phases come. Hence the opportunity for extra stimuli to become effective grows less and less, and these stimuli will also have to be stronger than is necessary when the pulse is slow. If then we find numerous extra-systoles with a rapid pulse, it is perhaps of more serious import than with a slow pulse, because then either the stimuli must be stronger or the excitability of the cardiac muscle greater. Christ <sup>(11)</sup> has also recently referred to the fact that the heart becomes regular during work. Lommel (*loc. cit.* p. 33) mentions a case which was very puzzling to him; it was one of extremely high frequency with paroxysmal tachycardia, where extra-systoles occurred only during the attack. It is to be hoped that he will some day publish the tracings of this case. This condition might be of great importance in solving the question of the mechanism of paroxysmal tachycardia (*cf.* § 73).

§ 23. **The Extra-systole in Pathology.**—The extra-systole plays an important part in the irregularities of the heart, as we learn daily from clinical experience. It is, therefore, absolutely necessary, from a clinical point of view, to become acquainted with this phenomenon, and the conditions under which it occurs, as far as

possible. Although the importance of the practical results obtained from this knowledge is not always the same, yet every one must admit that a careful study of this subject, a thorough investigation into the conditions under which it occurs, the forms in which it may appear, its cause and clinical features, is necessary before we can hope to make practical use of this knowledge.

In the first place it is a remarkable fact that the regular automatic rhythm of the heart is not affected by the ordinary extra-systoles that proceed from the auricle and ventricle. It is, therefore, not the heart itself that is irregular; there must be some external factor present which disturbs the regular rhythm. This fact is in itself of great importance. There is surely a great difference (as I have said before <sup>(118)</sup> p. 196) between a man who now and then makes a false step, stumbles, or limps because he has some disease of his lower extremities, and another who, although his legs are quite sound, stumbles when he is walking over rough ground, sharp stones, or steps into a deep hole! And it is particularly important to prove that extra-systoles are really present, because the irregularities to which they give rise may completely spoil the regularity of the pulse. When we consider that with numerous extra-systoles pure intermissions may arise, and also intermissions with more or less perceptible extra-pulse beats (so-called "bigemini"), and that the latter may follow the preceding pulse-beat with more or less rapidity and are followed by pauses of unequal length: when we reflect that the post-compensatory pulse is usually larger, and the one following it smaller, than the average, that extra-systoles may be grouped together in the most varied forms, and their pulse-waves may interfere with the dicrotic waves, it at once becomes clear that so great irregularity is found in these cases that one might readily think there was some serious cardiac lesion. The analysis of the pulse then shows that the original rhythm of the heart remains unchanged; in many cases no pathological change can be made out, and the organ is acting in a most satisfactory manner. In such cases it is not right to say there is *Arhythmia*, in spite of the irregularity, the inequality, and intermission of the pulse; the rhythm of the heart has remained the same. I have already suggested the name *Pararhythmia* or *Rhythmus perturbatus* for such cases. But, not to multiply names (as will be discussed more fully in the section on *Pulsus*

*bigeminus*), we may simply speak of *Extra-systoles*; the name is a correct one and cannot give rise to confusion.

§ 24. **Subjective Symptoms of Extra-systoles.**—It is usually not a difficult matter to diagnose extra-systoles in a patient. If one counts his pulse, and can go on counting, when the irregular beats occur, without losing the rhythm, it is almost always a case of extra-systoles. Moreover, the symptoms of which the patients complain usually lead one to think of them. They perceive the extra-systole as a thud in the cardiac region or within the chest and in the neck. And frequently they distinctly feel the stopping of the heart during the pause (they often say, "if that is possible"), and I have the impression that they are also conscious of the large blood-wave of the post-compensatory systole. These patients become very often slightly giddy for a moment. Yet it must be pointed out that some patients have none of these symptoms, and remain quite unconscious of the irregularity of their heart.

It is easy to understand the connection between these subjective symptoms and the extra-systoles, when once we have learned the physiology of the latter. The cause of these symptoms lies in the disturbance of the circulation and the abnormal mechanism of the extra-systole.

§ 25. **The Mechanism of Extra-systoles.**—When an ordinary contraction occurs very early in irregular movement of the heart it cannot drive the blood-stream much forward, because the contractility is not yet fully restored and the heart is still incompletely filled. The effect of the extra-systole on the circulation must be far greater. For here a non-physiological stimulus arises, not at the venous ostia, but in the wall of the auricle or ventricle. If the ventricle is stimulated it will contract first, and the auricle after, whether it is made do so by the physiological stimulus or by the one conducted from the ventricle to it. The filling of the ventricle, which is usually effected by the preceding contraction of the auricle, will, therefore, be very incomplete. The conditions are very unfavourable for the ventricle to empty itself when it is imperfectly filled and has still little contractility. The aorta has just been filled and the pressure in it is still very high. The effect of the extra-systole on the circulation will, therefore, be very little. The auricle cannot then empty itself in the usual way, and there follows a long pause with no contraction. The first effect of a ventricular extra-systole, therefore, will be a stasis of the blood in

the great veins, and a deficiency of blood and diminished pressure in the arteries. It is, therefore, not surprising that some patients suffer from temporary anæmia of the brain and hence a short attack of giddiness. The deficiency of blood in the arteries is shown most distinctly in almost every pulse tracing (*cf.* <sup>118</sup> Fig. VI.).

When the extra stimulus arises in the auricle, and the extra-systole proceeds from it through the heart, its mechanism may come nearer to the normal. The filling of the ventricle, which then does not contract till after the auricle, will possibly be more complete, and the compensatory pause may be shorter. But then the outflow of blood from the veins may be hindered. The extra-systole of the auricle may determine the contraction, but it may also happen, as it does with ventricular extra-systoles, that the extra-systole meets the normal contraction that is being conducted from the great veins. The effect of this on the stasis of blood in the veins has been studied and illustrated in a most admirable manner by Mackenzie <sup>(75)</sup> from the venous pulse in man. Cushny and Matthews <sup>(12)</sup> have contributed some experimental work to the further study of this condition; a theory which may help to explain it was mentioned in § 14 and recently published elsewhere.<sup>(124)</sup> It will depend on the time and place of stimulation what the effect on the venous pulse will be.

The mechanism of extra-systoles that arise from the auricle or ventricle at an irregular time can explain the objective signs of the "abortive" or "premature" systoles which have long been the subject of investigation. Hochhaus and Quincke <sup>(51)</sup> have given the fullest description of these signs; a loud "booming" sound is heard during systole on auscultation, and the shock of the extra-systole is frequently felt as a particularly strong impulse against the chest wall. These symptoms are remarkable for this reason, that the effect of this apparently strong contraction upon the circulation is so slight, and frequently none at all. The loud "booming" first sound is mainly due to the sudden tension of the mitral valves; when the extra-systole occurs early, the aortic valves are still under a high pressure; the ventricle, which is imperfectly filled and accordingly contracts quickly, will not be able to empty itself into the aorta, and will therefore strike the mitral valves with all the greater force. It is also possible that, with the diminished resistance to the contraction of the ventricle from imperfect filling of that chamber, the contraction may have a totally different result

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and produce a totally different muscle sound, which gives the booming character of the first sound.

The stronger apex impulse can be likewise easily explained. The normal cardiac impulse, as we know, is due to the fact that the heart is extended on the great vessels during systole, and hence strikes against the chest wall and remains pressed against it by the stiffening of the aorta as long as the ventricle continues to empty itself into the aorta (systolic plateau). During an extra-systole now the ventricle cannot empty itself, or does so very imperfectly; the heart is rapidly extended on the still full great arteries, because there is very little resistance to the contraction in the ventricle itself, and the impulse against the chest wall is also great because the aorta is scarcely opened; the apex impulse will also be strong but short in duration, because no blood is poured into the aorta, and the ventricle therefore is not kept pressed against the chest wall (absence of systolic plateau).

When we record the action of the heart we can expect the typical cardiogram of an extra-systole to show a quick rise of considerable height, corresponding to the apex beat, but followed immediately after by a fall, because the heart does not remain pressed against the chest wall (absence of systolic plateau). We can also expect that this cardiogram comes nearer to that of a normal contraction, the later the extra-systole appears after the preceding systole, and according as it is the auricle and not the ventricle from which the extra-systoles proceed.

As a matter of fact the character of the cardiogram of an extra-systole is just as we expect. For instances of this I may refer in the first place to the work of earlier observers, such as Rosenstein (<sup>98</sup>, p. 89, Fig. 12), Knoll (<sup>98</sup>, Plate IV., Fig. 6), Hochhaus and Quincke, (<sup>61</sup>) and Rodet. (<sup>96</sup>) The figures from the works I have just quoted readily show the peculiarities of these contractions which did not escape the observation of these authors. In works of most recent date, such as those of Mackenzie, (<sup>75</sup>) D. Gerhardt, (<sup>86</sup>) Lommel, (<sup>72</sup>) and Quincke, (<sup>90</sup>) the peculiar form of the cardiogram is treated more fully, and the question specially brought forward, whether it is possible to determine from the cardiogram if the extra-systole proceeds from the auricle or the ventricle. It may be expected that the well-known small elevation at the beginning of the systolic rise in the cardiogram, which is attributed to the contraction of the auricle, is absent in extra-systoles of ventricular

origin, but is present in those of auricular origin. Lommel had made some very good observations on this question, and in certain cases has been able to draw almost definite conclusions as to the origin of the extra-systole. But it can be readily imagined that it is not always possible to do this; for in a normal cardiogram the auricular elevation is often absent, and when the extra-systole begins at the auricle it need not produce any auricular elevation; the presence of such an elevation is also determined by the point and the moment at which the auricle is stimulated.

In the plates at the end of this book some of the figures demonstrate this very well. In Fig. 1 (Plate I.) the cardiogram is recorded above the pulse-tracing; 1-10 are extra-systoles; the abrupt rise of the curve in the former is very plain; the auricular elevation, which is quite distinct in the normal beats and is marked at three of these by small arrows, is entirely absent in most of the extra-systoles. In the extra-systoles 4, 5, 8, and 10, however, there might be some doubt whether it is an elevation due to the auricle or one caused by instrumental defect. The systolic plateau is not absent in the extra-systoles; this corresponds with the late appearance of the extra-systole and the not insignificant pulse-wave that is sent into the arteries. The ease with which the heart empties itself, even when the extra-systole occurs early in the diastole, is also explained in this case by the exceedingly low blood-pressure which also manifests itself in the pulse by its great dicrotism (*cf.* § 15).

In Fig. 7 (Plate II.) the systoles marked 1-5 must be regarded as extra-systoles. All of them show the abrupt rise of the curve; the auricular elevation, which is scarcely perceptible even in the normal systoles, is absent altogether in them; 1 and 5 rise very high, but sink again at once. There is no systolic plateau; 2, 3, and 4 do not rise so high; the broader the systolic plateau becomes, the less is the height of the wave. The connection is obvious. In 1 and 5 no blood is forced into the aorta, hence the strong impulse of the ventricle against the chest wall and the absence of the systolic plateau; in 2, 3, and 4 more blood is sent into the aorta, the apex tracing therefore does not rise so high, but the ventricle is pressed longer against the chest wall as it empties itself into the aorta. The absence of any extra beat in the accompanying pulse tracing at 1 and 5, and the presence of a distinct one at 2, 3, and 4, bear out this view, which is in part based upon the results obtained by Mackenzie. It was impossible to determine with certainty

whether the extra-systole proceeded from the auricle or the ventricle in this case, because the auricular elevation is absent and, at any rate, the rhythm of the heart was irregular.

It is frequently impossible to determine from the cardiogram the origin of the extra-systoles, or, indeed, the question whether they are premature normal beats or extra-systoles. If the rhythm of the heart is regular, the compensatory pause will throw some light on the matter; but if the heart is irregular, the question becomes more difficult, and still more difficult when the extra-systoles proceed from the venous ostia, when there is no compensatory pause and the mechanism of the extra-systole may be exactly the same as that of the normal contraction. An example of this kind is found in Fig. 5 (Plate II.) which was referred to in § 18. On looking at this pulse tracing one will at first think that the three long periods at the beginning of it are due to extra-systoles, and will do so all the more readily because numbers of these apparently can be seen throughout the tracing. But if it is compared with the cardiogram it will be seen that a second beat occurs only during the second period, and again at the fourth, which is a little shorter. On looking at the effect of the systoles on the pulse, one will be inclined to take those marked 1, 2, 3, 5, and 6, and perhaps also 7, 8, 9, 11, and 12 in the cardiogram for extra-systoles. Yet if one looks for the signs of extra-systoles here, it is quite impossible to distinguish between an extra-systole and a premature normal systole. In the majority of the systoles just alluded to the auricular elevation is indeed more distinct than in many of the normal systoles. Lommel has made a similar observation; this makes it improbable that they are extra-systoles. Besides, in shape these systoles are simply rounded off: they do not show any abrupt rise, or any diminution in the systolic plateau. There are all sorts of transitions between physiological contractions and extra-systoles such as we are discussing, but the pauses following them give absolutely no clue to their interpretation. It seems to me that it is impossible to determine whether the differences here are caused by the irregular rhythm, or whether extra-systoles really do occur; at all events we have no right to accept the latter view without further consideration (*cf.* §§ 77-83).

In cases where such doubt arises the venous pulse may perhaps give some information, as H. E. Hering rightly observes, because it sometimes records the movements that take place on the

right side of the heart. Lommel (*loc. cit.*) does not lay much store by this method of investigation. D. Gerhardt <sup>(85)</sup> has done some research in this direction, and in a few cases found an auricular wave in extra-systoles with a shortened compensatory pause. And so far his research is of some value, although it is very far behind the magnificent work done by Mackenzie. In 1894 he gave a most valuable contribution to the analysis of the venous pulse in his first paper, <sup>(74)</sup> and in his recently published book <sup>(75)</sup> his work in this direction is simply marvellous. He has collected such a wealth of material, he has analysed it with such critical acumen and correctness, and has set forth his results so clearly and logically that all who interest themselves in this subject must become acquainted with Mackenzie's work, and will be able to follow all his arguments without any difficulty. He has not touched on the physiological explanations of these phenomena, but he has supplied material of the greatest value for this explanation by his studies, in which sometimes he was able to record the four chambers of the heart simultaneously. He has given especially good examples of the abnormal mechanism of extra-systoles, which he continues to call by the name of "premature beats" (*cf.* § 69).

The "premature beats," which have been described by this name, or as "abortive" (*frustrane*) contractions, or "systoles avortées" by the authors just mentioned, and by others, such as Dehio, Stoitscheff, Riegel, and Lachmann, and which all presented the same features, must for the most part be undoubtedly regarded as true extra-systoles. And it may be observed here that the form of pulse usually called the *pulsus bigeminus* depends on the occurrence of extra-systoles (*cf.* § 69). Quincke has recapitulated the signs of "abortive" systoles in his most recent work on the subject; these signs are just the same as those described for extra-systoles. His explanation for the abnormal mechanism of these "abortive" systoles is as follows (*loc. cit.* p. 10): "These differences in form may perhaps be explained on the ground that a stimulus arises in the ventricle itself, not at the auriculo-ventricular groove, proceeding from here along the wall of the chamber as the normal stimulus does, but either at several points simultaneously or at some totally different place, such as the apex of the heart." This explanation, which Quincke puts forward for the abnormal mechanism, is exactly the same as that given for extra-systoles, for which there is so strong proof. And yet he will not admit that the abortive

contractions and extra-systoles are the same. I have never quite understood why he refuses to accept this view, for their identity is quite remarkable. The only argument that seems to support his theory is that the tracings obtained by Engelmann and Hering from the frog's and the mammalian heart "afford no means of distinguishing between normal and early occurring systoles, as cardiograms of abortive contractions in man show."

This objection of Quincke, however, proves nothing. A tracing of the frog's and the mammalian heart is obtained in experiments by the method of suspension, or Hering's method, by which the shortening which the cardiac muscle undergoes during contraction is accurately registered. With the extra-systole, too, only the shortening of the muscle is recorded. By this method, moreover, Cushny and Matthew discovered changes in the course of the contraction. But in a cardiogram it is not the shortening of the cardiac muscle, but something quite different that is recorded; it is not the tracing of a contraction that we get here, but that of the movement of the apex of the heart against the chest wall, which is only partially due to the shortening of the muscle, and is for the most part determined by the amount of blood in the great vessels. The difference, which Quincke lays stress on, between the contraction curve of an extra-systole in an exposed heart, and the tracing of the human heart, is, therefore, self-evident, and one cannot deduce an argument from it in order to find a difference between the extra-systole obtained in experiments and abortive contractions.<sup>1</sup>

Nevertheless, I must point out, as I have already done in my first paper on this subject,<sup>(18)</sup> that one cannot take abortive contractions and extra-systoles of the heart as always identical, as Lommel (*loc. cit.* pp. 36, 42) has recently done. It has been repeatedly pointed out that extra-systoles need not be abortive, and may produce an ordinary pulse-beat, while abortive contractions which cause a very small pulse-beat, or none at all, must not necessarily be extra-systoles. I would refer again to what has already been said in this paragraph about Fig. 5 (Plate II.), and to §§ 77-83. In interpreting pulse tracings of various kinds one must always pay attention to this: it is not infrequently very difficult or, indeed, impossible to determine whether one has to deal with extra-systoles or early occurring normal contractions.

<sup>1</sup> Cf. R. Tigerstedt in *Ergebnisse der Physiologie*, I., p. 241.

§ 26. **The Causes of Extra-systoles.**—Extra-systoles are produced in experiment by all kinds of stimuli, electrical, thermal, mechanical, and chemical, provided they act directly upon the heart. It is, therefore, natural to attribute the spontaneous extra-systoles found in man and many animals (*e.g.* the horse, dog, &c.) to direct stimulation of the heart-muscle. Indeed, the direct stimulation of the cardiac muscle was an idea entertained by the authors Knoll<sup>(62)</sup> and Rosenstein,<sup>(98 99)</sup> who, thirty years ago, worked at the premature contractions, which are now known as extra-systoles.

In 1872 Knoll (*loc. cit.* p. 226), following the trend of physiological thought at that time, wrote: "It must be left yet quite undecided whether we must regard this phenomenon as the result of some action on the muscular fibres or on the motor-nerve apparatus. Yet the idea, that these peculiarities in the heart's action on raising the intra-cardial pressure must be regarded as the expression of a stronger stimulation of the heart, is favoured by the fact that the very same phenomena are found in the heart's action when it is excited by a direct mechanical stimulus or by a very weak induction current."

It has been placed beyond all doubt, by the numerous experiments of Engelmann and many others, that there is direct stimulation of the cardiac muscle in extra-systoles. The nerves have a positive or negative influence on the automatic action of the heart; but they are unable to set up a contraction by transmitting motor stimuli to it, as the motor centre can in a voluntary muscle. H. E. Hering lays particular stress on this fact. After pointing out (<sup>40</sup> p. 26) that it has never yet been possible to produce an extra-systole "by the stimulation of the purely nervous structures that are connected with the heart," he comes to the conclusion that very probably "every bigeminus, trigeminus, &c., no matter where it arises, is myogenic in character."

If one takes into account only those forms of bigeminus and trigeminus that are produced by extra-systoles, one can fully agree with what Hering says. We will, nevertheless, have to decide, especially with regard to clinical work, to what extent nerve influence can be an indirect cause of extra-systoles. In the first place, it is not impossible that the power of automatic stimulus-production rises so high in one or more places in the heart wall that an effective stimulus is generated at that point now and then before the usual

stimulus has arrived from the root of the heart. Any auricular or ventricular contraction set up in this way by an autochthonous and not any extraneous stimulus would behave exactly like an extra-systole. Engelmann was the first to express this idea and point out such a possibility. If now the automatic action of the heart were considerably increased by a positive chronotropic nerve influence, extra-systoles might be set up in that way by nerve influence. Engelmann does not think this impossible.<sup>1</sup> F. B. Hoffmann does not believe in this chronotropic influence of the nerves on the ventricle, and he bases his position on his well-known and complete series of experiments on the innervation of the frog's heart (<sup>56</sup> p. 440). He thinks the chronotropic nerve fibres all run to the sinus, and none go so far as the auricle and ventricle. This question, which Lommel also refers to (*loc. cit.* p. 27), must, therefore, still be regarded as undecided. But the bathmotropic influence of the nervous system on the cardiac muscle is of much greater importance as a cause of extra-systoles. The excitability of the heart can be raised so much by this influence that feeble stimuli, which normally are unable to produce a contraction, set up an extra-systole in the hyper-sensitive muscle. And this brings us to the question which is so important in clinical medicine, viz., how far nerve influence can open up a way for the occurrence of extra-systoles, a question which Lommel has discussed so exhaustively and accurately that I wish to allude to his work here.

In discussing the causes of extra-systoles the following questions may now be asked :—

1. Extra-systoles are produced by extraneous abnormal stimuli ; what is the nature of these stimuli ?
2. The occurrence of extra-systoles is favoured by an abnormally high excitability of the cardiac muscle ; under what circumstances does this abnormal excitability arise ?

We must seek an answer to these two questions in the first instance in experimental physiology and pathology. When we look around for facts which might possibly give a solution to them, it is surprising that, in spite of the numerous experiments that have been made since Traube's time, there is a very great deal that requires elucidation, and that a decisive answer to our question cannot yet be given. In experiments where the heart was directly stimulated the matter is quite simple, but whenever more indirect stimuli are applied, we do not know whether those stimuli act on

<sup>1</sup> *Vide* Appendix 2.

the heart directly or whether they raise its excitability directly or indirectly. This applies particularly to the results obtained by the method of raising the intra-cardial pressure for the production of extra-systoles, a method much in vogue since the time of Traube and Knoll, and one which was again employed by H. E. Hering a few years ago. This method therefore is not suitable for arriving at the solution, because the enormous rise in blood-pressure obtained by clamping the great vessels or the abdominal aorta puts the heart in many respects under abnormal conditions. Of course it may be assumed that the high intra-cardial pressure stimulates the heart directly, yet it is also possible that the great pressure raises the excitability of the muscle, *e.g.* by stretching it; and possibly the excitability is reflexly raised by the increased pressure or by clamping the great vessels. As a matter of fact we are not one whit nearer the solution of this question than Knoll was in 1872, when he said <sup>(62)</sup>: "Although we have seen from what has been said, that the causes of the irregularities in the heart's action that appear on raising the blood-pressure are to be sought for in the heart itself, and that the cardiac inhibitory apparatus takes no part in producing this condition, we have not by any means arrived at a full knowledge of the ultimate causes of these irregularities. It must still remain a moot question whether this condition should be regarded as the result of some influence on the muscular fibres or on the motor-nerve apparatus of the heart." If we merely substitute the word "reflex" for "motor" in this last sentence, it holds good even yet. And Rosenstein in 1877 observed quite rightly <sup>(67)</sup>: "Wherever the resistance to the action of the heart increases, no matter whether this resistance arises *directly* from mechanical obstructions in the circulation, either at the ostia, in the muscle itself, or in the lungs, or whether it comes *by reflex channels* (either through the splanchnic nerve, as is probable in Riegel's case, or by irritation of sensory nerves and the consequent irritation of the vasomotor centre, or by the direct stimulation of the latter), and where *the excitability of the heart is at the same time increased*, the *pulsus bigeminus* can occur."

This uncertainty, which still exists in the production of extra-systoles by raising the blood-pressure, is present in the same way on attempting to work out the exact effect of other stimuli. It is perfectly certain that chemically active substances can stimulate the heart into extra-systoles; it is well known that they occur in

digitalis poisoning. But, even after the most recent researches, we can still ask the question: Does digitalis stimulate the cardiac muscle into contraction directly, or is the rise in blood-pressure produced by the administration of this drug the cause of the extra-systole? or is the excitability of the heart directly or indirectly raised? or does the digitalis tend to build up stronger autochthonous motor-stimuli at certain points in the wall of the heart? These questions may be raised with all cardiac poisons, and if we then consider how the blood-pressure is controlled by nervous influences, and that an increase in this pressure, and hence perhaps extra-systoles also, can be produced by stimulation of the vasomotor nerves, we can see that the number of questions that have to be answered in order to arrive at a final decision on this matter is beyond calculation.

By the perfectly accurate and well-thought-out method which Engelmann and others have employed for investigating the excitability, contractility, and the other cardiac functions, we are enabled to arrive at an answer to these questions. The analysis of the action of the various poisons on the functions of the cardiac muscle has fortunately been already taken up by several workers, and I would particularly refer to the experiments of Walther Straub,<sup>(106)</sup> from which, as will be seen later on, he has discovered facts of the greatest importance for the analysis of the irregular pulse. The experiments of Biedermann, Loeb, Göthlin, and Straub<sup>(107)</sup> in particular, on the action of simple chemical substances and of ions on the automatic movement, excitability, contractility, and conductivity of cardiac muscle appear to offer better promise towards the solution of the fundamental problems than the otherwise equally important experiments on the action of extremely complicated bodies like alkaloids. And the question which we previously raised, as Lommel too has done, whether it is possible for abnormal stimuli to interfere with the physiological, and thus set up a double rhythm, may perhaps be solved in this way.

§ 27. **The Clinical Significance of Extra-systoles.**—From what has been said we see that, with the exception of those cases in which a stimulus is directly applied to the cardiac muscle, we do not yet exactly know what is the cause of the contraction in extra-systoles even in experiment. How, then, will it be possible to analyse the complex conditions leading to the occurrence of extra-systoles in man, and to state which of the direct stimuli in any given case are

to be taken as the cause of this phenomenon? How shall we ever be able to employ a rational treatment for this abnormality of the heart's action?

Fortunately in practice we do not need to condemn ourselves to merely looking on, although we are not yet able "to discover the causes of things." It is very seldom that we are able to remove the causes of disease; in few cases can we speak of a real "rational" treatment. And yet with the experience that we have gained, we can often successfully remove injurious predisposing factors; we can bring favourable influences to bear on the case, and, by various measures, bring about a rapid improvement. Nevertheless we must always strive to increase our knowledge of the disease, always keeping in view the attainment of a rational form of treatment.

We must endeavour in this instance, too, to discover the causes of the disease, and some possible means for its removal. We can make some progress towards this end by collecting the cases and noting the circumstances under which extra-systoles occur. Further, an attempt may be made to find out the conditions under which they can be made to disappear. Finally, analogous cases must be sought out from physiology and experimental pathology, and the phenomenon of extra-systoles split up, where possible, into its component parts by the help of these.

From the clinical side valuable contributions on arrhythmia of the heart, and especially on extra-systoles, have been given by Henschen,<sup>(30)</sup> Heubner,<sup>(45)</sup> Ebstein,<sup>(17)</sup> Mackenzie,<sup>(76)</sup> Lommel,<sup>(72)</sup> and others (to mention only the works of recent years). I myself have taken up more the physiological side of the question, and gathered together facts from this field. The results of these researches are still very indefinite; yet it is hoped that, by careful analysis of the various forms of cardiac arrhythmia, we shall be able some time to arrive at more satisfactory conclusions.

Extra-systoles occur at all ages, under the most varied conditions, in healthy individuals and in those seriously ill, in apparently strong persons as well as in the weak. Their frequency is no more connected with any particular extrinsic circumstances than with intrinsic. Hence it is, generally speaking, impossible to determine their clinical significance or estimate their diagnostic and prognostic value. Each case must be taken on its own merits. Still the principal fact remains that extra-systoles in themselves possess no diagnostic significance, and that no conclusion can be drawn from their

mere presence as to any particular form of cardiac disease; all that they prove is merely that the heart is disturbed in its rhythm, and stimulated into extra contractions by abnormal agencies.

Those persons, however, that suffer from extra-systoles may be arranged into certain groups, and the cases classified on a somewhat loose system. With such a classification it is most striking that very young children rarely exhibit extra-systoles. Every one can prove this for himself, and indeed Mackenzie goes so far as to speak of a "youthful" and an "adult" type of arhythmia, the latter showing the presence of extra-systoles. I am not prepared to go so far, for I have often been able to make out extra-systoles in children, although I admit they are more often found in older people. These older patients may be conveniently arranged in several classes.

The first class is formed by persons who not only do not suffer from any organic disease of the heart that can be detected, but do not show a single symptom of impairment of its force; in fact, they look in perfect health, and do not suffer from any other complaint; they are persons who suffer from extra-systoles only now and then throughout the whole of their life, live to a normal age, and after their death do not show any peculiarity in the heart-muscle that could give even a plausible explanation for the occurrence of extra-systoles. Almost all writers who take an interest in this subject are unanimous in confirming this fact; I myself know several persons of this kind, and have frequently been consulted by other medical men who observed extra-systoles in themselves, and thought them a very alarming symptom. In this class of healthy individuals one can hardly imagine that there are always abnormal pathological stimuli present capable of producing extra-systoles, while the excitability of the cardiac muscle is normal. In my opinion one would rather think of some abnormally high excitability of the heart, either congenital or perhaps acquired. Just as there are some classes of animals, such as the horse and the dog, in which extra-systoles are met with much more frequently than in others, and just as in a large number of frogs there are often only a few that will give a positive result with Goltz's experiment, so there may be some persons with very easily excited hearts, and others whose hearts are less easily excited; such an idea is certainly not without analogy in the case of other organs. Stimuli, that cannot have any effect on other people, are able to set up extra-systoles in those persons who

may have possessed this excitability hereditarily or acquired it in their youth from some injurious influences.

In many individuals the condition is obviously not merely one of increased excitability, but may go on to "irritable weakness" (*reizbare Schwäche*); every clinician is acquainted with such people, whose hearts (and often other organs as well) are easily stimulated into excessive activity, but are just as quickly exhausted, and ultimately become unfit for work on the slightest physical exertion. Here we enter the field of real pathology, and we must bear in mind that this irritable weakness of the nervous system is a second cause of cardiac arrhythmia in the great class of "neurasthenic" individuals, because in them the heart is influenced through reflex channels by much weaker stimuli than in persons with a strong, less easily excited nervous system. This may also afford an explanation of the undeniable fact that in neurasthenic people extra-systoles may arise from purely nervous influences—a fact which, as Lommel points out, is not inconsistent with the myogenic character of the extra-systole.

A second class is composed of persons in whom the extra-systoles are produced by causes which have no direct connection with the heart or circulation. We must also place those cases in this class in which pathological changes in other organs exert a reflex chronotropic or bathmotropic influence on the cardiac muscle, or those cases where toxic substances, which can stimulate the muscle directly, are circulating in the blood. Every physician knows very well that diseases of the stomach or intestine, even simple chronic constipation, or the presence of intestinal parasites, may first manifest themselves by the appearance of extra-systoles; if the disease is cured, the stomach emptied, the constipation corrected, or the parasite expelled, the extra-systoles all disappear like a flash. Was it toxic substances, absorbed from the intestine, that acted on the heart-muscle directly, or was there some reflex proceeding from the intestinal tract that predisposed to the occurrence of extra-systoles? Arguments could be adduced in support of both these views. It is well known that toxic substances are absorbed from the alimentary canal; but we know from experiment as well as from experience on the operating table, how easy it is for reflexes proceeding from the abdominal organs and the peritoneum to influence the action of the heart. Extra-systoles are observed over and over again in cases where there is absolutely no

doubt that toxic substances are present in the body, *e.g.* in various infectious diseases. It is remarkable that in them the extra-systoles most usually appear during the convalescent period. An explanation of this may be found in the fact that in many infectious diseases other organs do not become affected till the febrile stage has passed off, as is seen in post-diphtheritic paralysis and post-scarlatinal nephritis. In the case of the heart the fact that it is most exhausted and perhaps also most excitable after the disease conduces to the late occurrence of extra-systoles; the symptoms of "irritable weakness" in the heart are seen after every bad case of infectious disease. Moreover, the slower rate of the heart during convalescence perhaps accounts for the fact that extra-stimuli are effective during this period which could not have any effect with the frequent pulse of the febrile stage (*cf.* § 22). Perhaps this is in keeping with an observation which I was often able to make, and which others too possibly made, *viz.*, that while extra-systoles are of no grave significance during convalescence, they make the prognosis very bad when they come on in the febrile stage, *e.g.* in the first few days of a croupous pneumonia, and point to a very serious condition of the heart. Further clinical observations are bound to throw light on this subject, while experimental research must as surely find a solution to the questions that were stated above and have never yet been solved.<sup>1</sup>

A third class is composed of persons in whom there is some disturbance in the circulation, although the heart itself is not seriously affected. Increased blood-pressure would first be thought of, because we know that in experiments this is a cause of extra-systoles. There are arguments in support of the view that even in man a high blood-pressure can set up extra-systoles. Since the thorough experiments of Von Basch<sup>(2)</sup> it has been ultimately recognised that the knowledge of the arterial pressure in man may be of the highest importance for an insight into diseases of the heart and vessels, and that Von Basch's instrument in its later form, the tonometers constructed by Gaetner, Rivarocci, Oliver, and others, as well as the splendid experiments of Von Recklinghausen<sup>(31)</sup> and Oliver<sup>(32)</sup> will not fail to give us in a few years most valuable information on the condition of the blood-pressure in man. Lommel has

<sup>1</sup> I am therefore of the opinion that the time has not yet arrived, when we can really draw inferences as to *prognosis* from the various forms of arrhythmia, as Rehfisch recently sought to do at the Medical Society of Berlin (*cf.* Deutsche Med. Wochenschrift, 1903. Nos. 20 and 21).

given in full detail all that is known of this in relation to the occurrence of extra-systoles. I would merely point out here, that although it has been proved beyond doubt that extra-systoles occur very frequently with a high arterial pressure, the relation between the two has not yet been determined. The questions stated in § 25 will have to be settled by experiments before we can venture to speak with any certainty on this matter. The words of Knoll and Rosenstein which we quoted before, that extra-systoles can occur with a high blood-pressure as well as under certain conditions, are still as true for the clinician as for the experimental worker. I may give the following as an example: It is an undeniable fact that persons suffering from arterio-sclerosis have a strong predisposition to extra-systoles. I was once for four years medical officer in an institution for aged people, where 75 men and women, varying from 60 to 95 years of age, were kept under the most favourable conditions possible. Extra-systoles were so often met with in them that I fitted up my kymograph there to enable me to take tracings every day. Although the extra-systoles in many of these cases disappeared again, they very frequently returned with any slight complaint and even any nervous excitement (indeed in many old people a *choc des opinions* may be enough). It is natural to think that the arterio-sclerosis, which was often very marked in these old people, had something to do with the occurrence of extra-systoles. Yet it is by no means proved that the extra-systoles were produced by the high blood-pressure which frequently accompanies arterio-sclerosis. It is equally possible, and perhaps more probable, that the excitability of the heart-muscle may rise considerably as a result of their great age. This idea is supported by several facts: (1) That other signs of excessive excitability of the heart (*delirium cordis*, cf. §§ 77-83) are very frequently met with in elderly people; (2) By the fact that in young people, as well as in the old, extra-systoles may occur in great numbers when the blood-pressure is very low; and (3) by a fact to which too little attention is paid, viz., that the diseases which are accompanied with very high blood-pressure are, generally speaking, not the ones in which extra-systoles are most often found, e.g. chronic nephritis. If uræmia supervenes in a case of nephritis, we then find extra-systoles very frequently, but we know too that in such an event all the organs, the heart-muscle included, are greatly irritated by abnormal products of metabolism retained in the circulation or by the high mole-

cular concentration of the blood. I am not averse to the use of Lommel's expression "relatively too great resistance," but I think it is more likely to further our knowledge in this direction if we recognise that we do not yet know the connection between these phenomena, and that we must wait for further experimental work to elucidate it; in the meantime, we can collect clinical material to help us in solving this problem.

This third class may, perhaps, also include those cases where extra-systoles occur on altering the position of the body. We have already heard of cases in which there were no extra-systoles on sitting or standing, but whenever the patient lay down they appeared (§ 22). This phenomenon may be partly due to the slower rate of the heart on lying down. But it is often so well marked, even on the patient's changing from his back to his side, and *vice versa*, that one naturally thinks of some abnormal mobility of the heart, to which Determann, A. Hoffmann, and others have given special attention. It is certainly possible that with an abnormally heavy or movable heart a change of position caused a blocking of the circulation in the great vessels, which acted as a stimulus in producing extra-systoles. I was very much struck with the fact that they were extremely well marked in the cases of probably true bigeminy of the heart, which were already described in § 21, and will be discussed more fully again in § 68. I do not believe, however, we are yet in a position to give a full explanation of the phenomenon of extra-systoles.

Finally, a fourth class of persons suffering from extra-systoles comprises patients that have real organic disease of the heart. And in this class also it is true that the extra-systoles are in themselves of no diagnostic value in relation to the stage or extent of the cardiac lesion. It does not require any proof that the various affections of the heart, *e.g.* dilatation, inflammation, poor blood-supply to the muscle, over-exertion, can all provide stimuli to set up extra-systoles either directly or reflexly. And it is no less true that these abnormalities are not always bound to produce extra-systoles. We often see the very worst cases of heart disease, that lead shortly to the death of the patient, go on without any sign of extra-systoles, and particularly cases of real acute myocarditis, which go on with a high and increasing frequency to the end without the slightest disturbance of the rhythm. This statement is at variance with the old theory that arhythmia is a sign of cardiac disease. That it is

not so, however, is being more and more generally recognised, and is sufficiently proved by what has been here said; and in literature one finds more and more authors (*cf. e.g.* Josserand and Gallevardin<sup>61</sup>) supporting the statement that extra-systoles do not occur in acute myocarditis where one indeed should expect them most. In serious affections of the heart, therefore, we are still ignorant of the conditions that determine the presence or absence of extra-systoles.

After all that has been said, clinicians ought not to attach much significance to extra-systoles in themselves, and yet ought to consider it worth while to examine every case and see if a cardiac lesion is present or not, whether there are any conditions (and they must very often be looked for outside the heart) present, and what these conditions are, which can set up extra-systoles either directly or indirectly. The first duty in treating the patient will be to remove these conditions. A uniform line of treatment naturally cannot be laid down.

#### THE DISTURBANCES OF STIMULUS-CONDUCTION.

§ 28. **On Disturbances of the Individual Functions of the Heart.**—Since the thorough physiological experiments that were described in Chapter I. were made, we know that the rhythmical movement of the heart results from the combined action of the four great functions of its muscular fibres, viz., automatic stimulus-production, excitability, the power of conducting the stimulus from muscle-cell to muscle-cell, and contractility. Knowing this, we can at once expect that if any one of these functions is in abeyance or changed in any way the rhythm of the heart will suffer; and we might also expect that certain typical disturbances of rhythm will occur with any such change. And this is actually what happens. Certain disturbances of the cardiac rhythm induced experimentally can be referred to disturbances of certain functions. The disturbances of stimulus-conduction were first known, probably because they are most easy to demonstrate and measure. The contractility is measured by the size of the contraction, and a mass of valuable experimental material on the disturbances of this function has been obtained. But we are also able, chiefly through the most recent work of Engelmann and others, to determine and measure the dis-

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turbances of stimulus-production and excitability by means of appropriate methods, and there is also promise of further progress in this direction in the next few years (*cf. e.g.* <sup>28</sup>).

The next step, naturally, was to inquire whether there are irregularities of the heart in man that correspond to the definite types obtained from experiment, and can be attributed to certain disturbances of function. Such an inquiry shows that there really are certain disturbances of rhythm which can with the greatest probability be referred to definite changes of functions, in the same way that extra-systoles obtained by experiment could also be proved to occur in the higher animals and in man. In most cases there is a disturbance of several functions at the same time, although in rare cases one can observe an affection of one function, either alone or predominantly. There is no doubt, I think, that when several observers take up this subject, and make a careful observation and analysis of each individual case by itself, instead of merely putting together all the forms that bear a superficial resemblance to one another, as is done at present, the types of disturbance of certain functions will be met with not so very infrequently and generally recognised. A great advance will thereby be made in arriving at a rational diagnosis of the functions of the heart, and a number of new points revealed on which to base the treatment of disorders of these functions.

#### § 29. The Disturbance of Stimulus-Conduction in Experiment.

—The motor stimulus, as we know, normally arises in the wall of the heart at the *venæ cavæ*. From this region it is conducted through the heart, thereby stimulating the different chambers in succession. The rapidity of conduction, therefore, can be determined from the progress of the wave of contraction. Where the length of the contraction-wave was denoted in Engelmann's terminology by  $\lambda$  it was thought expedient to denote the conductivity or power of conduction by  $\Lambda$ .

The changes in the rapidity of conduction can be studied most easily at those places where it is always slowest, viz., at the points of junction between the chambers. For this purpose physiologists usually employed the auriculo-ventricular groove, and examined the interval between the auricular and the ventricular contraction.<sup>1</sup> The slowly dying frog's heart is the most suitable to experiment

<sup>1</sup> Shortly put, the interval  $A$ — $V$ .

with; as the asphyxia becomes more and more marked, and makes  $\Lambda$  less, the progress of the contractions becomes slower, and the interval  $A_s - V_s$  greater. When the auricle and ventricle are separated, and their movements registered side by side, as is easily done by means of the suspension method, the length of the interval  $A_s - V_s$  and the changes in it can be accurately measured (*cf.* 18, 82).

$\Lambda$  is dependent, in the first place, on the presence of oxygen. When the heart is in a state of asphyxia, the administration of oxygen can recover the conduction considerably, even when it has sunk very low. We must refer here to Göthlin's work, mentioned in § 6, which proved that certain ions can influence the stimulus-conduction. Like the other functions,  $\Lambda$  depends greatly upon the systole of the heart and the work it has previously performed. Every systole robs the heart of its power of conduction; during the diastole this power is gradually restored again, but normally does not reach its maximum by the time the next systole begins. The frequency of stimulation has therefore an effect upon  $\Lambda$ ; but, at the same time, the number and strength of the preceding stimuli have an effect in the sense that strong and numerous stimuli reduce the conduction-power more than few and weak stimuli do. It must be observed, however, that only effective stimuli have a negative dromotropic influence; even the strongest stimulus has no such effect, when it comes on during the refractory phase and does not produce a contraction. The dromotropic effect, which can be produced either by direct stimulation of the nerves or by reflex channels, is also of the greatest importance from the clinical point of view; for when we diagnose the presence of dromotropic influences in our patients we must ask ourselves whether the cause of them is in the heart itself or is conducted to it through the nerves.

A great diminution of the conduction-power and its consequences can be best demonstrated, as we have already said, on a dying frog's heart at the interval  $A_s - V_s$ .

As the conduction gradually grows worse and worse this interval gets always longer; the conduction may become so bad that the ventricle does not begin to contract until just before the next auricular systole. Any one that had not followed the way in which this phenomenon slowly developed would think that the auricular systole followed the ventricular; in other words, that

there was a reversal of the usual order of contraction. But if  $\Lambda$  continues to grow worse, there finally comes a time when the stimulus is no longer conducted (or not with sufficient strength?),  $A_s - V_s = \infty$ ; in other words, the ventricle does not contract. During the pause that arises through the missing of this systole, however,  $\Lambda$  will have plenty of time to recover again so far that the next stimulus is again conducted to the ventricle, and it contracts; but after a few systoles have occurred,  $\Lambda$  is again so much reduced that another beat is missed. In this way a ventricular contraction may continue to be dropped after the same number of systoles for a considerable time, thus producing a regular intermission of the ventricle. A very beautiful example of this missed ventricular systole is given in Fig. 11 (Plate III.); the tracing was obtained from a frog's heart, and was taken from Engelmann's paper on the Conduction of Stimuli.<sup>(18)</sup>

At a later stage of asphyxia, auricular contractions soon drop out in consequence of the defective conduction from the sinus to the auricle. Examples of this condition are shown in Fig. 10 *a*, and 10 *b* (Plate III.); both these figures were taken from tracings that were kindly lent to me by Engelmann. In Fig. 10 *a*, the auricular and ventricular contractions are missed after every five beats; in Fig. 10 *b* after every three. The numbers appended to these figures (in  $\frac{1}{3}$  sec.), show that the interval  $A_s - V_s$  is shortest immediately after the pause, and grows longer as the number of contractions increases. In Fig. 10 *a*, for example, the interval  $A_s - V_s$  at the end of a group of five beats is nearly twice as long as the interval at the beginning of the same group.

The contractions of the heart are thereby made to appear in groups which may assume a very complicated form from further interference with the conduction-power and the other functions. In these cases we speak of the "periodic" action of the heart, and the groups are called after their discoverer "Luciani's periods."

§ 30. **First Case of Disturbance of Stimulus-Conduction in Man.**—Now and then we observe in the pulse in man groups of beats which result from the regular falling out of a beat. A regular intermission of this kind can be produced, as was fully explained in § 20, by the regular occurrence of extra-systoles. Yet it suggested itself to inquire whether the formation of groups of contractions can also arise in man from an interference with

conduction. Muskens was the first to specially indicate such a possibility, after his attention had been drawn to the significance of disturbances of conduction during his researches on the action of the heart. <sup>(82, 83, 84)</sup> In 1899 I proved that in some cases disturbances of conduction must distinctly be taken as the cause of this grouping, and that other forms of allorhythmia as well can be produced by the same cause. We will now give a description of the cases that I have already reported, <sup>(119, 120, 121)</sup> and others of the same kind that have not hitherto been published.

The first case (*see* <sup>119</sup>) was that of a female, aged forty years, of nervous temperament, who had long observed that her pulse did not beat regularly. She had a weak circulation, but exhibited no other lesion of the heart than slight dilatation. She was delicate and anæmic; a few years later she began to suffer from attacks of real gout; perhaps this gouty tendency was manifesting itself even then. Her pulse was small, soft, and showed a continual intermission after every three or at most six beats, usually after every four or five. The heart-sounds were weak but pure. The most striking point was that extra-systoles, which are otherwise nearly always seen in an intermittent pulse, were absent altogether in this case; besides, none of the subjective symptoms of extra-systoles, mentioned in § 24, were present. In the pulse tracings, which are here reproduced (Figs. 12, 13, 14, Plate III.), the small extra pulse-waves which give the appearance of a *pulsus bigeminus* are nowhere to be seen. Extra-systoles could be excluded with certainty as the cause of the intermission in this case.

If now we measure the pulse period (a period = the distance between two successive equal phases of the heart's action, =  $T$ ; a period at the radial artery therefore =  $T$  rad.), we find a condition that is at first puzzling and very complex; in every pulse group the radial periods show a considerable variation in length; moreover, every intermission is distinctly shorter than was expected, *i.e.* shorter than twice the length of the preceding periods. In this example of well-marked arhythmia of the pulse it is found, on comparing the groups with one another, that this arhythmia is repeated regularly in every group, a *rhythmical arhythmia* or *allo-rhythmia* is in fact produced. Each intermission is followed by a period that is much longer than the others; the succeeding periods of the same group are distinctly shorter, but usually increase slightly in size up to the next intermission: the period immediately after

this intermission again is the longest, and so on. The size of some groups is given as follows :

In  $\frac{1}{10}$  seconds.

$T$ rad. 1 =	9	$9\frac{1}{4}$	$9\frac{1}{2}$	9	9	$9\frac{1}{2}$	$9\frac{1}{2}$
$T$ rad. 2 =	$7\frac{1}{2}$	8	8	8	$7\frac{3}{4}$	8	$7\frac{1}{2}$
$T$ rad. 3 =	$14\frac{1}{4}$	$8\frac{1}{2}$	$8\frac{1}{2}$	15	8	$14\frac{3}{4}$	$7\frac{1}{2}$
$T$ rad. 4 =	—	$14\frac{1}{2}$	$14\frac{3}{4}$		$14\frac{1}{4}$	—	$14\frac{1}{2}$

These and other numbers given on the tracing prove beyond doubt that the regular action of the heart is here being disturbed by a constant injurious influence. This is a *negative dromotropic* influence, as is found on comparing this pulse carefully with the action of the ventricle of the frog's heart while beating in Luciani's periods.

If we observe now the interval  $A_s—V_s$  in Luciani's periods (cf. Plate III., Fig. 10 *a* and 10 *b*), we see that, while the first ventricular systole after an intermission follows the auricular most quickly (the interval  $A_s—V_s$  is shortest), and is most powerful ( $\Lambda$  having most time to recover itself during the pause), the conduction power is more exhausted with that first systole than with any other in the group; the succeeding contractions affect  $\Lambda$  only a little more. This fact is confirmed in all Engelmann's tracings and tables. The increase of  $A_s—V_s$  in Fig. 10 *a* and 10 *b* proves this beyond doubt. That we have really to deal here with an inherent property of cardiac muscle, and not with a mere accident or some special property of the fibres forming the block at the auriculo-ventricular groove, is proved by a muscle experiment described by Engelmann elsewhere,<sup>(20)</sup> although he does not draw particular attention to the fact. A portion of the wall of the ventricle is excised, and cut into two parts in such a way as to leave a bridge of muscle between them. If now both parts are suspended, and one of them receives an electrical stimulus while the point of stimulation and the contraction of both are recorded,  $\Lambda$  can easily be estimated from the time between the moment of stimulation and the contraction of the distal half. The tracings and tables which Engelmann gives of this experiment all show that  $\Lambda$  is most interfered with after a long pause, most through the first systole, and only a little more through the succeeding ones; the interval is shortest at the first contraction after the pause, it is considerably longer at the second, and increases only a little

more in length with the succeeding systoles. The following figures (in  $\frac{1}{10}$  secs.) are taken from the tracings in Engelmann's paper.

Interval after 1st stimulation	2.6	2.4	2.2	2.2
„ 2nd „	3.6	2.75	3	2.7
„ 3rd „	4	2.9	3	3
„ 4th „	4.5	3.1	3.1	3.1
„ 5th „	4.8	3.2	3.2	3.4

These figures show clearly that the greatest damage is done to the conduction-power by the first systole.

The influence which this peculiarity of the reduction of conduction-power has upon the period of ventricular contraction ( $TV_s$ ) can be easily demonstrated by means of a diagram of the heart's

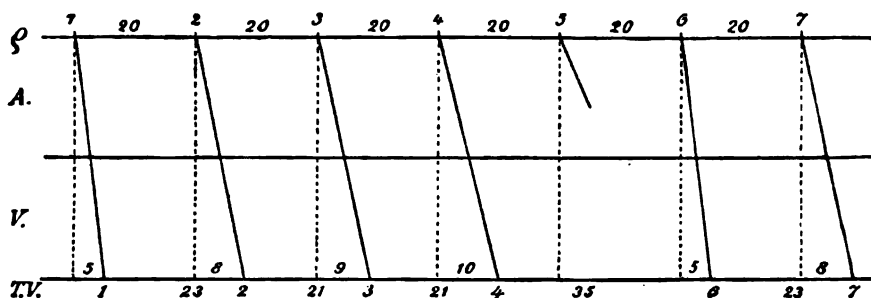


FIG. XII.

action. Let the period of the contraction stimulus at the root of the heart,  $T\rho = 20$ , the interval  $\rho - V_s$  in the most favourable condition, *i.e.* after a pause, = 5, and at the extreme limit, when the stimulus is still conducted with sufficient strength, = 10. During the contractions the interval  $\rho - V_s$  is increased from 5 to 10, and on analogy of the experiment we may then assume that after the first systole  $\rho - V_s$  is increased, say by 3, and after each of the succeeding systoles by 1. In the accompanying diagram, Fig. XII., the time is given on the abscissæ, the period of the motor stimuli at the root of the heart ( $T\rho = 20$ ) on the top line, the second horizontal line represents the auriculo-ventricular groove, while the bottom line shows the period of ventricular contraction ( $TV_s$ ) as it varies with the effect upon the conduction from  $\rho$  (the root of the heart), through  $A$ , the auricle, and  $V$ , the ventricle.

If  $A$  remained constant with every systole, as it normally does,

$TV_s$  would naturally be  $= T\rho$ , even if  $\Lambda$  was very bad; a uniform delay in the conduction would produce a uniform lengthening of  $TV_s$ . But now, when each systole has a different influence on  $\Lambda$ , it is quite different: in the present example, the lengthening of the interval  $\rho - V_s$  by 3 will make  $T_1 = 23$ , and its subsequent lengthening by 1 will make  $T_2$  and  $T_3 = 21$ . But then the limit is reached, the fifth stimulus is either not conducted at all or not in sufficient intensity, and an intermission is the result. Since the interval  $\rho - V_s$  returns again to 5 during this pause, the length of the intermission ( $T \text{ int.}$ ) will be 5 less than the double of  $T\rho$ , i.e.  $T \text{ int.} = 2T\rho - 5 = 35$ . After the intermission the same thing is repeated.

This discussion shows how variations in the interval  $\rho - V_s$  are able to change the rhythm of the ventricle very considerably, while that of the physiological stimulus retains its regular rhythm. In a frog's heart that is beating in Luciani's periods, this form of ventricular rhythm which we have here analysed recurs again and again with almost mathematical precision. In Fig. 10 *a* and 10 *b* (Plate III.) the corresponding  $TV_s$  in each group is the same to within  $\frac{1}{10}$  sec. In Fig. 10 *a* the  $TV_s$  measures in four groups (in  $\frac{1}{10}$  secs.):—

	I.	II.	III.	IV.	V.
$T \text{ int.}$	76.5	76	75.5	76	76
$TV_{s,1}$	56.5	57	56	55.5	—
$TV_{s,2}$	50	49.5	49	49.5	—
&c.	46.5	46.5	47	46.5	—
	47.5	47.5	47	47	—

At the same time it must be remembered that small errors cannot be avoided, as the commencement of  $A_s$  and  $V_s$  cannot always be determined with perfect accuracy, that  $TV_s$  is independent of the interval  $\rho - V_s$ , and that only the interval  $A_s - V_s$  could be estimated here, so that  $TV_s$  does not correspond exactly altogether to the interval  $A_s - V_s$  which was here found. It will be observed that  $TV_{s,2}$  is still a little greater than the following  $TV_s$ , and  $TV_{s,3}$  is the least.

If now we compare the tracing of the regularly intermitting pulse in our patient with the condition of the frog's heart just described, we arrive at the astonishing result that the regularly recurring irregularity is exactly the same in them both, and in the steadiest part of the pulse tracing the regularity is almost as great as in the frog.

Moreover, in this tracing the first  $T$  rad. after the intermission ( $T$  rad.<sub>1</sub>) is always the greatest, while the intermission is always distinctly less than twice that of the preceding or average pulse-periods (*cf.* the numbers in Fig. 12, 13, 14, Plate III.).  $T$  rad.<sub>2</sub> is usually the least, while the succeeding periods are again slightly longer.

The figures obtained from the pulse tracing naturally cannot help us to calculate the absolute amount of  $\Lambda$ ; but we can obtain some relative values, and particularly the loss of  $\Lambda$ , from them.

When a heart intermits after every four systoles, then every fifth beat will have no effect (intermission). One group with one intermission, therefore, corresponds to five contraction stimuli. The length of  $T\rho$  will therefore be  $= \frac{1}{5}$  of the length of the whole group. This may be expressed as follows, when  $n$  = the number of contractions in one group :—

$$T\rho = \frac{TV_{e1} + TV_{e2} \dots + TV_{em} + T \text{ int.}}{n + 1}$$

In our diagram it would be represented so :—

$$T\rho = \frac{23 + 21 + 21 + 35}{4 + 1} = \frac{100}{5} = 20.$$

If we apply this formula to the pulse tracing in Fig. 14 *b*, we find (in  $\frac{1}{18}$  seconds) for the first group—

$$T\rho = \frac{9.33 + 7.75 + 13}{3 + 1} = \frac{30.08}{4} = 7.52 ;$$

for the second group—

$$T\rho = \frac{31}{4} = 7.75 ;$$

for the third group—

$$T\rho = \frac{29.50}{4} = 7.375 ;$$

for the fourth group—

$$T\rho = \frac{36.80}{5} = 7.36 ;$$

for the fifth group—

$$T\rho = \frac{38.25}{5} = 7.65.$$

If, therefore, we know  $T\rho$ , we can calculate how long the intermission ( $T$  int.) would be if  $\Lambda$  were constant,  $T$  int. being  $= 2 T\rho$ . But the shorter  $T$  int. is than  $2 T\rho$ , the longer does the interval  $\rho$ — $V$ , become through reduction of  $\Lambda$ . This difference also tells

how much more slowly the contraction passes over the heart, *i.e.* how much  $\Lambda$  has been lost. This may be expressed as follows:—

$$2 T\rho - T \text{ int.} = (\rho - V_s)n - (\rho - V_s)_1 = \Lambda n - \Lambda_1.$$

If we apply this formula to our diagram (Fig. XII.) we find—

$$2 \times 20 - 35 = 10 - 5 = 5.$$

If it is applied to our tracings the result is, for the first group—

$$2 \times 7.52 - 13 = 2.04 \left(\frac{1}{10} \text{ sec.}\right);$$

for the second group—

$$2 \times 7.75 - 13.25 = 2.25 \left(\frac{1}{10} \text{ sec.}\right);$$

for the third group—

$$2 \times 7.375 - 13 = 1.75 \left(\frac{1}{10} \text{ sec.}\right);$$

for the fourth group—

$$2 \times 7.36 - 12.8 = 1.98 \left(\frac{1}{10} \text{ sec.}\right);$$

for the fifth group—

$$2 \times 7.65 - 13 = 2.30 \left(\frac{1}{10} \text{ sec.}\right).$$

The increase of  $\rho - V_s$  and diminution of  $\Lambda$  can be calculated for each pulse period of a group in the same way as for the intermission. If  $n$  denotes the number of the period in a group that we wish to find, then—

$$TV_m = T\rho + (\Lambda_{n+1} - \Lambda_n).$$

The reduction of  $\Lambda$  is therefore—

$$\Lambda_{n+1} - \Lambda_n = TV_m - T\rho.$$

For example, the decrease of  $\Lambda$  in the third period of our diagram is—

$$\Lambda_4 - \Lambda_3 = 21 - 20 = 1.$$

In Fig. 14 *b* we can estimate the decrease in  $\Lambda$ , for example, for each period in the first group as follows:—

For the first period—

$$= 9.33 - 7.52 = 1.81 \left(1 = \frac{1}{10} \text{ sec.}\right);$$

for the second period—

$$= 7.75 - 7.52 = 0.23 \left(1 = \frac{1}{10} \text{ sec.}\right);$$

$$\text{Together} = 2.04 \left(1 = \frac{1}{10} \text{ sec.}\right).$$

This number exactly corresponds to the total reduction of  $\Lambda$  which was calculated from the shortening of the intermissions.

The lengthening of the interval  $\rho - V_s$ , and the reduction of  $\Lambda$ , is therefore a measurable and fairly constant quantity. We must not, however, attach too much importance to the numbers here given,

In the first place,  $T\rho$  is only an average estimate in these calculations, and with a nervous patient during examination with the kymograph certainly not so constant as in a quietly dying frog's heart.

In the second place, the interval  $\rho-V$ , and  $\Lambda$  cannot be estimated exactly in one pulse tracing, for when  $\Lambda$  grows less, and the contraction accordingly passes more slowly over the heart, the wave of blood will be driven into the artery and propagated with somewhat less rapidity, and will be felt a little later in the radial artery. This late arrival of the radial pulse was not taken into account in this case, and must therefore be subtracted from the figures that were obtained.

It is proved that the wave of blood is transmitted through the arteries more slowly by the fact that at the end of a group the pulse curve rises a little less abruptly than at the beginning of it. This is a proof of the diminished *celerity* of the pulse. If we examine the tracings carefully for this, we find that these peculiarities are all explained by the slower progress of the contractions.<sup>1</sup> In Fig. 14 *b* we have endeavoured to measure this slower ascent of the curve by the time-marker.

The comparison of this abnormal pulse with its physiological prototype may be continued in further detail.

Experimental research has shown that  $\Lambda$  is diminished (it has less time to recover) when the frequency of stimulation and contraction is increased. *Ceteris paribus*  $\Lambda$  is diminished with an increased rate of heart. If we wish to find out whether this is also the case in our patients, we must bear in mind that it is hardly possible to raise the frequency of the stimuli alone in them; for besides that the excitability or at least the intensity of the stimulus, the blood supply, and therefore the supply of oxygen and the nutrition of the cardiac muscle, will probably always be affected, *e.g.* by physical exertion, as well. All these factors might change, or indeed obscure, the secondary negative dromotropic effect of the higher frequency. What do we find now in our patient in this respect?

In the steadiest part of the tracing, where  $T\rho$  is greatest, the intermissions occur usually with least frequency, which thus agrees with experiment. Moderate exertion on the part of the patient

<sup>1</sup> In reproducing the tracings this condition, which was very distinct in the original, has unfortunately not been quite accurately copied.

was followed at first by greater frequency, larger groups, and therefore fewer intermissions: for example, one group of eight continuous beats with  $Tp = 6.68$  was recorded. But immediately after this stage of increased frequency there followed a stage of exhaustion, in which the negative dromotropic effect of the increased frequency made itself very manifest, and the intermissions occurred in much greater number, frequently after every two beats, while the length of the period was 7.75. Fig. 13 (Plate III.) was taken from the second stage; and as it shows, the pulse returned after a time to its usual allorhythmia of an intermission after every four or five beats.

When it is realised that a heart with much diminished  $\Delta$  recovers slowly under suitable treatment, it is to be expected that the intermissions will gradually appear less frequently, separated by larger groups of systoles, but at the same time the first  $T$  rad. after the intermission will always be longer than the others. When still further improvement is made, the intermissions will finally disappear altogether and be replaced by a regular pulse.

In the present case it was really possible to observe the improvement in the heart in this way, as was thought probable from the start. The first pulse tracing (Figs. 12 and 13) was taken on May 14, 1898. After a long rest, nourishing food, and a change in the country, the patient was again examined, and intermissions were found less frequently (Fig. 14 *a* and *b*). When she presented herself again (on October 23), to allow of pulse tracings being taken, the regular rhythm of the heart had been restored and the regular intermission had disappeared (Fig. 15).  $T$  rad. was about 8.6 (tenths of a second), *i.e.* only a little more than the average of the intermitting stage.

§ 31. **Second Case of Disturbance of the Conduction.**—I was recently able to take tracings of another case, which will be dealt with again in § 32. The case was that of a man suffering from uræmic coma, who died two days afterwards. The uræmic symptoms varied every moment in intensity and form, and in the same way the condition of the pulse was also a very variable one. It was, generally speaking, a frequent pulse; it beat now and then with half frequency, but in the intervals showed frequently for a considerable time the form of allorhythmia that is seen in Fig. 16 (Plate IV.). The tracing was taken by means of a Jacquet's sphygmograph, and therefore shows the time in  $\frac{1}{4}$  seconds.

A glance at Fig. 16 and the numbers accompanying it shows

at once that exactly the same allorhythmia is present in this, as in the first, case. The commencement of the tracing shows the pulse beating with regular frequency; it then passes into a form of allorhythmia with several intermissions, and the regular intermission soon appears; each intermission is less than two periods combined, the first period after the intermission is too long, the second too short, then comes the normal period, and after four or five beats an intermission again occurs.

A considerable difference in the height of the pulse-waves is observed in this tracing. The first beat in every group is distinctly higher, and the second distinctly lower, than the average pulse-wave. The small second beat might induce one to think it was an extra-systole; but it is fully shown in § 66 and the succeeding paragraphs, and in §§ 77-83, that this is impossible, and besides this small wave is followed by a very short pause. A secondary inotropic effect would be a more likely thing to think of: the contractility of the heart could have time during the pause to recover to a large extent, and the systole would be a very strong one; after this very strong contraction the heart would be unable to recover so quickly, and thus the second systole would be small. But we do not need to introduce such an influence to explain the difference in the pulse-waves; that is satisfactorily done (1) by the secondary inotropic effect of the large preceding systole; and (2) by the variation in the filling of the heart and the arterial system that accompanies the allorhythmia. After the pause the heart is well filled with blood, and the strong first contraction drives the blood into the arteries. Before the second systole the filling will be much less complete; the arterial pressure will still be higher (as is shown in the sphygmogram, by the diminished fall of the line), and so the second pulse-wave is a small one; by the third systole the filling of the heart has returned completely, or almost completely, to its former condition.

In this case, therefore, we can only consider the diminution of conduction as the cause of the allorhythmia. In the same patient a stage was also observed in which the conduction was very much increased. For the sake of clearness this latter stage will be discussed again (§ 33).

§ 32. **Third Case.**—A third case, which has already been reported,<sup>(120)</sup> showed great loss of conduction-power, and is very instructive on that account.

A labourer, æt. 50 years, had suffered from influenza; he had recovered from this attack, but remained weak, unfit for work, and was greatly exhausted by the slightest exertion. He had no organic lesion of the heart. When he was sent to me by another doctor, he presented a pulse which was regularly intermittent after every two to four beats. Next day a pulse tracing was taken, and his pulse showed still further changes in the rhythm. The intermissions occurred not only singly but frequently in couples. A portion of this tracing is reproduced in Fig. 17, *a* and *b*.

If we look at this tracing, and turn our attention in the first place to those points where the intermissions occur singly, and compare them with the tracings of the previous patients, as described in the preceding paragraphs, we find that they are exactly similar. In all three cases the intermissions are too short, and the inequality of the *T* rad. in each group appears in the same order. Not a single extra-systole can be detected here either from the sphygmogram or by auscultation; the cardiogram, which is reproduced in Fig. 17 *c*, Plate IV., shows that the heart was in perfect rest during the pause. There can be no doubt that here also loss of conduction-power was the cause of the intermissions.

But this pulse tracing differs from the previous ones in the fact that two intermissions occur immediately after one another again and again. This is probably to be interpreted in this way, that during the first intermission,  $\Lambda$  has recovered only sufficiently to conduct *one* stimulus but not *several*. It is not till after the second intermission that  $\Lambda$ , which, as we know, is very largely dependent on the number of the preceding systoles, is so far restored again by the double pause that several stimuli in succession can pass through the cardiac muscle, and several systoles appear after one another. In this case the conduction-power of the heart has suffered more than in the previous cases. This is proved by the fact that with a slower rhythm the intermissions occur with greater frequency, and there are seldom more than three or at most four systoles in each group. Only one group of five beats could be seen throughout the whole of the sphygmographic examination. The length of the *T* rad. in this group and of the intermissions accompanying it was (in  $\frac{1}{10}$  seconds):—

39.5—25.5—22.25—23—22.5—43, and so on.

If we calculate the average period, or, more correctly speaking, the rhythm of stimulus production at the root of the heart from the

length of the  $T$  rad. and the intermissions, we find that it varies from 21.5 to 23, i.e. from .86" to .92."

The fact that the first intermission is always shorter than the second shows that  $\Lambda$  is restored most, though not quite completely, during the first intermission, and is increased to a less extent during the second. This is the reverse of the fact that was fully discussed in the first case (§ 30), viz., that the first systole of a group always injures  $\Lambda$  the most, while the succeeding systoles injure it very little more.

This action that is taking place in the heart may be better understood if we represent it in a diagram as follows:—

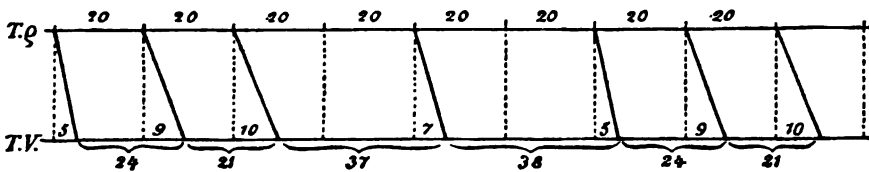


FIG. XIII.

Let  $T\rho$  (the period of stimulation) = 20, as in Fig. XII. § 30, the interval  $\rho - V_s$  in the most favourable case, at the beginning of a group, = 5, and at the point where the stimulus is still just transmitted = 10. From what we learned in the physiological experiments we will have to assume the first systole after the intermission injures  $\Lambda$  most, the interval  $\rho - V_s$  increases the most, indeed, more than in the previous case, so that  $\rho - V_s$  will be = 9. The next systole brings  $\rho - V_s$  to 10, but now  $\Lambda$  is too weak, the next systole is not conducted with sufficient force, and so a contraction drops out. During this intermission  $\Lambda$  does not recover sufficiently, so that  $\rho - V_s$  at the end of the intermission returns only to 7 instead of 5. The result is that the first stimulus can be conducted onwards, but not the second, and so another beat drops out. But now  $\Lambda$  can recover itself as far as this is possible,  $\rho - V_s$  on the first systole will now be = 5, and so the cycle goes on again, several systoles coming after each other, until  $\Lambda$  is exhausted.

The variation in the length of the interval  $\rho - V_s$  produces, as may be seen on the lower line (the ventricular systoles), an allorhythmia in the movement of the ventricle which corresponds exactly with our pulse tracing.

We cannot look for even an approximate estimate of the varying length of the interval  $\rho - V_s$  from the numbers given in



stimuli is converted into this remarkable form of allorhythmia, the origin of which, but for the knowledge of this variation, would remain a perfect mystery.

Moreover, a wrong interpretation of some of these forms of allorhythmia might easily be made. For example, the forms here described and shown in Figs. 12, 13, 17, 18 might be mistaken for bi- tri- and quadri-gemini. And there is no doubt that of the numerous pulse tracings, that were published before, some could well be attributed to a disturbance of conduction. But in the older tracings the time-marker is almost invariably absent, so that nothing can be said about them with certainty. If, for example, one reads Sommerbrodt's article (<sup>105</sup> p. 542), one finds a pause almost invariably after the fourth pulse-wave, and sometimes after the third or fifth. It is impossible to decide in the small figure without the time tracing whether there is a disturbance of conduction or not; this case is quoted here merely to show that forms of allorhythmia similar to those here described are perhaps not so rare as one might infer from the few cases I have reported. Riegel (<sup>94</sup>) also gives figures (*e.g.* Fig. VII.) which might well be included under this form of deranged function. Lommel (<sup>72</sup>) recently stated that he had observed cases of similar allorhythmia. It will be necessary, however, to make a careful analysis of each individual case in order to avoid confusion with other disturbances, and especially with extra-systoles.

§ 33. **Fourth Case.**—I come now to the description of another case, which I published before, and which I cannot help attributing to a great disturbance of conduction, although this interpretation of it is more open to criticism than in the other cases we have discussed.

The patient, at the time the pulse tracing was made, was a man seventy-four years of age, who was on the whole in perfect health for a person at his time of life. Very slight attacks of giddiness, and a passing feeling of constriction on breathing were the only symptoms that made him consult a doctor. His pulse was, however, a veritable treasure of different forms of allorhythmia. I found him with a regular infrequent pulse on only one occasion. Almost every day it was different, although a definite type could be recognised in it. Careful measurement of the pulse periods and comparison with the other cases confirmed the surmise that this was also a case of disturbance of conduction. Two forms of

F

allorhythmia in this pulse are exactly similar to the other three cases.

The first of these forms is shown in Fig. 18 *a*, Plate IV. Here we find a *regular double intermittent pulse*,<sup>1</sup> in which groups of three beats regularly alternate with two intermissions. The signs of a diminished conduction-power are distinguishable: the first *T* rad. of each group is by far the longest, the following ones are much shorter, and the intermissions are less than twice the length of *T* rad. The only difference from the double intermissions in the previous pulse tracing is that the first intermission is longer than the second.

The second stage of this tracing, which exactly corresponds to our first case, is formed by the part where two intermissions alternate with groups of only two beats, as in Fig. 17 *b*. This type of allorhythmia is more or less the normal rhythm in this patient. After all sorts of variations, the rhythm usually returns to this form; hence two tracings of this kind are here reproduced, Fig. 18 *b* taken in August 1898, and Fig. 18 *c* in October 1898. When we compare them with Fig. 17 *b* their similarity is at once apparent. But here, too, there is the same difference, that the first intermission is longer than the second. This can be explained on the ground that  $\Lambda$  recovers itself more during the first intermission. If we leave this difference out of account, the diagram in Fig. XIV. is exactly similar to these forms of allorhythmia.

And here and there we find *single* intermissions throughout the tracing, although certainly not so frequently as in Case I. Examples of these are shown in Fig. 18 *b* and *c* at  $\times$ . This very variation demonstrates clearly how the rhythmical stimulation of the heart goes on undisturbed even during the intermission, but as the conduction of the stimulus is generally defective the latter is ineffective.

In the large number of tracings, which were taken on different days, we can follow step by step how the intermissions increase in frequency as  $\Lambda$  gets weaker, the character of the allorhythmia becomes more and more obscured, and, finally, it approaches the condition of bradycardia.

In the same way as there are regular double intermissions we also meet with the *regular triple intermittent pulse*. An example of

<sup>1</sup> The accompanying cardiogram (Fig. 20) showed that no extra-systoles occurred during the long pause.

this is given in Fig. 18 *d*, where three intermissions regularly alternate with groups of three beats.

There are places in the tracing where four, five, or six intermissions occur in succession regularly. To avoid the too great multiplication of plates, these parts have not been reproduced; but, as examples, we append some figures (in  $\frac{1}{10}$  seconds) giving the length of *T rad.* in the separate curves:—

18—27.5—31—26.5—28—18—16—31.5—29—27.5—27.5—19.75  
—19, and so on.<sup>1</sup>

16—29—30.5—28—27.5—27—17.25—15—27.75—29.5—29.5—  
28—25.5—16.5, and so on.

In Fig. 18 *c* a stage is shown, where seven or eight intermissions regularly occur, with only two beats between them. On the same day Fig. 18 *f* was taken, and in it we can count *nineteen* intermissions before two beats in succession occur again. Here, again, we should note the signs of the defective conduction, viz., that the intermission is too short, and the first normal *T rad.* too long. It is also remarkable that where this large number of intermissions occurs, the first one is usually greater than the second, more in keeping with our first case.

One might now expect that the intermissions would ultimately appear so often that it would be no longer possible to see two pulse-beats in succession. And as a matter of fact I found this patient on one occasion with a perfectly regular pulse. The *T rad.* of this pulse corresponds with the length of the intermissions on other days, or rather was a little shorter. The pulse was observed for more than an hour, and had an average frequency of 56 beats per minute without once showing two beats occurring more quickly after one another. A portion of this tracing is given in Fig. 19. Thus at the end of the various forms of allorhythmia we find a condition of true *bradycardia*, the origin of which could certainly not have been suspected had we not been able to follow its development from the regular intermittent pulse step by step. Only every alternate stimulus is now transmitted from the root of the heart; the number of beats is therefore equal to half the number of motor-stimuli, and the period of ventricular contraction is twice that of the stimuli.

In reviewing again the changes in the cardiac rhythm that are due to a greater or less inhibition of conduction, we find in these

<sup>1</sup> The numbers corresponding to the intermissions are given in thick type.

four cases all forms of allorhythmia from the normal regular pulse-rhythm (Plate III., Fig. 15; and Plate I., Fig. 4 *a*), to the regular pulse of half frequency (Plate V., Fig. 19; and Plate I., Fig. 4 *b*). And the steps from one extreme to the other are: (1) the regular intermittent pulse with groups of seven, six, or fewer beats up to the alternation of one intermission with one normal period (Plate III., Figs. 12-14); (2) the intermissions begin to occur in twos (Plate IV., Fig. 17 *a*), and then occur regularly in twos (examples in Plate IV., Figs. 17 *a*, 18 *a*, *b*, *c*); (3) then come the forms with two, three, four, five, or more intermissions in succession, which merge ultimately into regular bradycardia.

When the action of the heart is so much deranged, we cannot expect perfect regularity. The conduction-power is then always about its minimum; a full or sufficient recovery of  $\Lambda$  is out of the question, a large continuous series of systoles is no longer possible, and it is easy to imagine that the slightest thing that is able to have a secondary dromotropic effect, *e.g.* increased work, or slight arrhythmia, may alter the form of the allorhythmia. These irregularities, which occur in cases of great disturbance of conduction, therefore cannot furnish any objection to the explanation we have here given, nay rather, they tend to support it. It is just these transition forms which show plainly that the motor stimuli are being produced during the intermission as well, because some of them are accidentally conducted now and then and produce a contraction (in Fig. 17 *b* and *c* at  $\times$ , and also in most of the other tracings). H. E. Hering has raised objections to my explanation of this case; he has proposed another, but I think it is wrong, although it is impossible to contradict it with absolute certainty (*cf.* § 37). I am therefore glad that I am able to quote another case in which it can be actually demonstrated that every second beat drops out.

It is very clearly proved by the pulse, which was already discussed in § 17, that the systole can drop out although the motor-stimulus is produced, a condition which is not only easily obtained by experiment but also occurs in man (see Fig. 4 *a* and *b*). The halving of the frequency in this case indeed makes it very probable that something similar happens where the frequency of the *regular* frequent pause is suddenly exactly reduced by half; but it was clearly shown that the motor-stimulus was present, by the fact that when an extra-systole occurs the compensatory pause always con-

tinues exactly to the middle of the second period and not to the end of it. And this form of pulse throws light on these discussions in a surprising manner, when we bear in mind that the pulse was obtained from the same patient as the case of disturbance of conduction described in § 31. The halving of the frequency was noted two days after Fig. 16, a typical tracing of the disturbance of conduction, was taken, and very shortly before the patient's death. When the proofs of this disturbance were so evident a short time before, it was obvious that one should point to the defective conduction-power as the cause of the missing of every other beat. Against this it might be argued, as H. E. Hering <sup>(43)</sup> has done in the cases which I previously published, that there was possibly also a diminution in the stimulus-production, the excitability, or the contractility. It is difficult to take up this question until we have specially described the disturbances of these functions; we shall, therefore, only observe here that the reasons why we cannot assume a disturbance of stimulus production and contractility in this case will be found in the special chapters of this book, in §§ 39-45 and 51-54. And in §§ 46 and 50 the question is discussed why it is not likely to be a disturbance of excitability, (if there is any in these cases it takes at most only a secondary place). One point, however, must be here emphasised: We are compelled to accept the inhibition of conduction as the cause of the various forms of allorhythmia just described by their complete similarity with the grouping that was obtained experimentally from this cause; and it gives a perfectly satisfactory explanation of these irregularities which would otherwise be unintelligible. It is not at all improbable that the other functions of the cardiac muscle may have also suffered; still, *this* form of allorhythmia can only be explained on the theory of an inhibition of conduction; it must, therefore, be held as the cause until a better explanation is given.

§ 34. **The Mechanism of these Forms of Allorhythmia.**—If we examine these cases further and reflect on them in the light of this explanation, the question is opened up whether the conduction was so much impaired throughout the whole heart that the auricle and ventricle both remained at rest during each pause, as in Fig. 10 *a*, Plate III., or whether there is only a dropping out of the ventricular systole, while the auricles go on pulsating as in Fig. 11, Plate III. I am unable to reply with *absolute* certainty for the above-mentioned cases: (1) because I had not yet fully appreciated

the importance of taking tracings from the apex beat and the venous pulse, as in Case I., and (2) because none of these patients showed a distinct apex impulse or any venous pulsation from which a tracing could be taken. And yet I think I can state with very great probability that in these four cases the auricular systoles were also missed, for these reasons:—

If the auricles continue pulsating while the ventricular systoles fall out, their pulsations can not only be observed in the venous pulse (see § 35), but can also be recorded in the cardiogram, in which an auricular elevation is usually to be found; and not infrequently they can even be heard (*cf.* § 35). Not one sign of an auricular systole could be found in any of these patients. In Case II. the patient was too restless to allow of a cardiogram or venous pulse being taken, but there were absolutely no cardiac sounds during the pause that could come from a contraction of the auricle. In Case I. there was no venous pulsation, but during the pauses of the heart not a sound could be heard even after the most careful examination with the phonendoscope. Neither in Cases III. and IV. could any auricular sounds be made out, and in the cardiogram not a trace of any movement could be seen. Fig. 17 c, Plate IV., is the cardiogram of the third patient. The cardiogram in Fig. 20, Plate V., which was taken from the fourth patient, proves that the heart was in perfect rest during the long pause.

We must therefore assume in these cases that both the auricular and the ventricular systoles are missed, and hence that the stimulus is not conducted onwards. Accordingly the result of the stimulus, the contraction, must be confined to the muscle-cells in which it had arisen, and also perhaps to the immediate neighbourhood. We cannot assume that this minimal contraction also drops out, for otherwise the stimulus-matter would not be destroyed; it would accumulate and cause merely a simple lengthening of the period, as will be discussed more fully in § 51, &c. It is not surprising, however, that this minimal contraction, which is confined to its place of origin, is not recorded either in the cardiogram or the venous pulse tracing.

But it has long been suspected with very great probability that there are cases in which only the systole of the ventricle falls out; or, in other words, the conduction is arrested at the auriculo-ventricular groove; and a great number of cases have now been recorded which prove this with certainty.

§ 35. On Systoles blocked at the Auriculo-Ventricular Groove.

—In § 29 it was described how the failure of conductivity in the cardiac muscle can be followed with perfect accuracy in a dying frog's heart, especially at the auriculo-ventricular groove; this failure ultimately becomes so complete that an auricular systole is no longer followed by a ventricular. For the details of this phenomenon (which has long been known as "heart-block"), I would refer the reader to the works of Engelmann, <sup>(18)</sup> Muskens, <sup>(52)</sup> Gaskell, and others. That this blocking is the result of a complete or incomplete arrest of the conduction is proved by the fact that one can actually see the lengthening of the interval  $A_1-V_1$  in experiment.

Against the objections that were afterwards raised by H. E. Hering, we must draw special attention to the fact that in many cases the arrest of the conduction can be proved to be the sole cause, and that the excitability or contractility is not seriously impaired. These two functions are frequently not affected at all, or only very slightly. It is true that the condition of heart-block has not yet been fully worked out, but all the facts of experiment go to show that the arrest of conduction is the primary cause. In this connection the recent work of von Kries <sup>(65)</sup> deserves attention. In it he describes the development of a condition of polyrhythmia in heart-block through a diminution of the excitability (produced by local cooling), and explains it on the ground that the frequency continues to be reduced by half, being brought in this way to  $\frac{1}{2}$ ,  $\frac{1}{4}$ ,  $\frac{1}{8}$ , &c., of the original frequency with the addition of a rhythm  $\frac{1}{8}$ ,  $\frac{1}{8}$ ,  $\frac{1}{8}$ , and so on, of the original rate. This shows also that, as the stimulus is always taking longer to reach the ventricle, and the conduction is being more and more delayed, the stimulus may finally reach the ventricle during its refractory phase. We must wait for further physiological research before it is possible to give a definite decision in this matter. Against this theory of von Kries it may be urged in the first place that, as the stimulus takes longer to reach the ventricle, its refractory phases are also longer in appearing, so that his ingenious explanation cannot be accepted off-hand. But apart from the question whether the dropping of the ventricular systoles can be explained in this way or not, his own figure bears out that the delay of conduction was the primary cause of the missed beat.

The occurrence of heart-block in man came first into general

notice after the communications of W. His, jun.,<sup>(49 50)</sup> on a case of Adams-Stokes' disease, in which he heard rhythmical sounds over the auricles during the long pauses of the ventricle. These sounds were due, as was proved by the venous pulse, to partial contractions, most likely contractions of the auricles. His could find only two previous cases, one observed by Gerhardt in his "Text-Book on Auscultation and Percussion," and the other by Chauveau.<sup>(10)</sup> I shall refer again to this second case, and shall merely mention the observations of Huchard, who, in his well-known *Traité des Maladies du Cœur*, remarks that in similar cases dull sounds can be heard during the long pause between the systoles, and these sounds he attributes to imperfect or abortive contractions. He speaks about "*bruits de cœur en écho*," but gives no further information to enable one to determine whether it was auricular contractions or extra-systoles that occurred. Similar observations were made by Quelmé<sup>(89)</sup> and Piatot.<sup>(88)</sup>

I myself have observed several cases of this kind, but, unfortunately, was never able to take any tracings of them. One case was that of an old woman who had attacks of extreme bradycardia, with a pulse-rate of 24-28 beats per minute. The heart-sounds were exceedingly weak, but none could be heard during the pauses. It was a remarkable fact, and one that supports the view here put forward, that the rate of the pulse did not rise slowly after the attack, but suddenly became three times as fast (75-78). Another case was much more convincing. A man, seventy-five years of age, was suffering, as was afterwards proved by the autopsy, from great cardiac hypertrophy, arterio-sclerosis, oedema of the lung and emphysema, bronchitis, and softening of the left frontal convolution. The patient became unconscious from the attacks, which became more and more frequent within a few days; the pulse at first disappeared on one occasion, it was counted, for 45 seconds, and then it returned again. The rate of the pulse during the attacks was nearly 28, sometimes 56. *When the rate was 28 a rhythmical venous pulse could be felt in the neck, regularly four times as fast as the rate of ventricular contraction.* Every fourth wave in the venous pulse was bigger than the rest, probably the result of the ventricular systoles. In other cases the disturbance is a very complicated one, as in Fig. 32, Plate VI. This tracing was taken for me by Professor Winkler of Amsterdam, and will be fully discussed in § 59. In this case also it is easy to see from the radial tracing that the heart does not remain

at rest during the exceedingly long pauses. In discussing the cases which Mackenzie has published, we shall find a proof that auricular contractions make these little elevations in the radial curve; it is therefore highly probable that heart-block is present in this case. Similar signs of auricular action can be seen in the radial tracings published by Webster<sup>(116)</sup>; they will also be discussed at greater length in the chapter on nerve influences.

A case, very similar to the second one I described, was published in 1902 by Lichtheim,<sup>(70)</sup> but, unfortunately, without any tracings.

a.



b.



c.



FIG. XV. After Mackenzie.

The patient was a man that had a pulse-rate of 32, and occasional attacks of syncope; he suffered from Adams-Stokes' disease. "In the neck pulsations of the jugular veins could be observed, besides the slow carotid beats, the former being much more frequent than the latter. A simultaneous tracing of the apex impulse, radial and venous pulses showed that for every arterial pulse there was one cardiac impulse, and, quite regularly, three venous pulse-beats."

I have not been able to decide whether Hoffmann's case<sup>(53)</sup> should be included under this variety of heart-block, as certain data have been omitted. An extremely important contribution to the subject of heart-block has recently been made by Mackenzie

(<sup>75</sup> chap. 27, p. 279, and <sup>76</sup> p. 1411). Through the kindness of this author I am able to reproduce his tracings in Fig. XV. *a*, *b*, *c*.

His patient was an elderly man, sixty-six years of age, who felt in fair health and was capable of considerable exertion. The rate of the heart varied to a great extent, viz., from 42 to 23 and 35. He had a slight but visible venous pulse. In Fig. XV. *a* we see the small elevations *a* due to the contraction of the auricle, which Mackenzie has studied very minutely, and the waves *c*, which are produced by the carotid. It is at once plain that *a* occurred with perfect regularity, yet only every alternate *a* was followed by a carotid wave and a radial pulse (lower tracing). Every second ventricular systole was missed; heart-block was present. In Fig. XV. *b* we see the same thing; but here two ventricular systoles fall out twice, only every third auricular contraction being followed by a ventricular. In Fig. XV. *c* the ventricular rhythm has become quite separated from the auricular, as will be discussed more fully again, but still the auricle goes on beating with perfect regularity.

Another case, which Mackenzie recently published in the *British Medical Journal*,<sup>(76)</sup> is no less convincing; it was the case of a man who had suffered from influenza. The tracings of this case also are reproduced here (Fig. XVI.). A mere glance at them suffices to show that ventricular systoles are now and then missed, while the auricle continues to beat with absolute regularity all the time. Figs. XVI. *c* and *d* are particularly instructive, for in them Mackenzie draws attention to a small elevation in the radial curve, which exactly corresponds with the systole of the auricle. From this Mackenzie shows (1) that auricular systoles may be recorded in a sphygmogram of the radial (and this is specially important for a right interpretation of my Fig. 32, Plate VI., and of Webster's figures, to which reference has already been made); and (2) that in this case of heart-block the right and left auricle acted together. He also proved, from the condition of the negative liver pulse (which he showed to be due to the contraction of the right ventricle), that the left ventricle did not act and miss a beat (missed the carotid and radial pulse-beat) alone, but the right ventricle acted and missed beats with it. So Mackenzie succeeded in recording the action of all the four chambers of the heart in man for the first time, and in establishing beyond doubt the complete heart-block, the continued action of the two auricles, and the simultaneous cessation of both ventricles. We are

under great obligations to this keen and clever observer for showing how this can be accomplished.

A clearer proof for the occurrence of heart-block in persons who were certainly not in the throes of death (Hering) cannot be

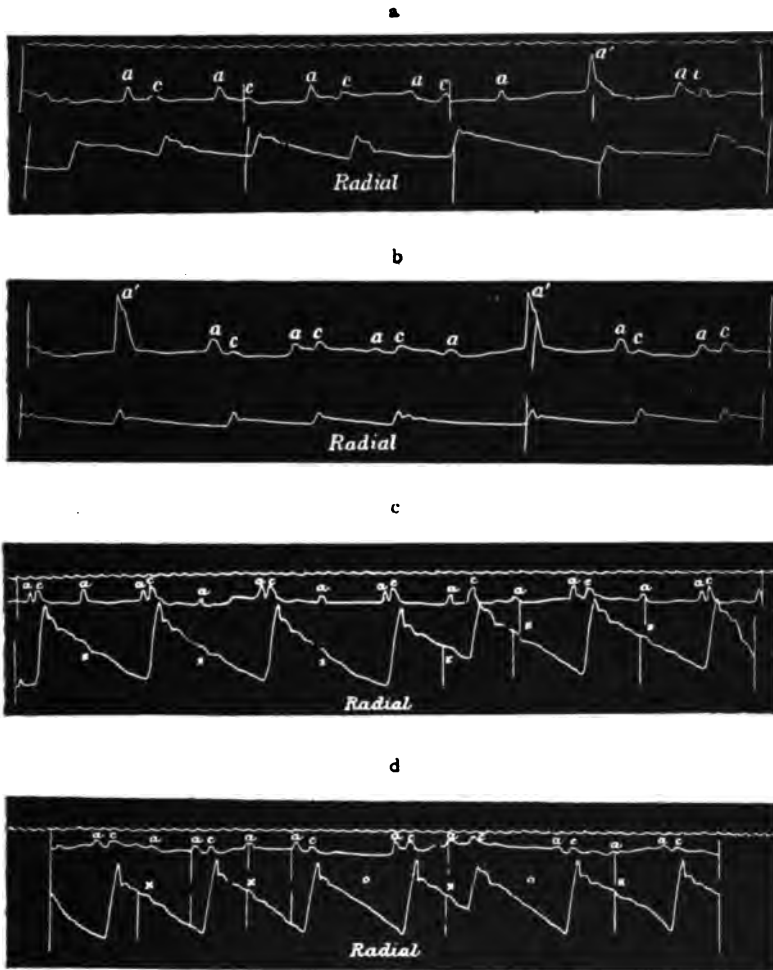


FIG. XVI. After Mackenzie.

desired. Another question, however, arises from the conditions in man himself, viz., Is it possible for the conduction of stimuli to be *completely arrested* at the auriculo-ventricular groove, either temporarily or permanently, and the circulation still to go on? This question must apparently be answered in the affirmative, for the following reasons: in Fig. XV. c, from Mackenzie, every third auricular

systole is not followed by one in the ventricle, but the two chambers go on, each in their own regular rhythm, independently of one another.

This phenomenon is explained by the old Stannius's experiment. When a portion of the heart is ligatured off from the rest, it begins to beat independently of the stimuli, that are no longer conducted to it; so here in the same way the ventricle, in virtue of its inherent power of automatically generating stimuli, continues its rhythmical action at a very slow rate. Mackenzie, who however does not accept the explanations given by modern physiologists, does not see any other way of explaining this phenomenon than by supposing that the ventricle takes up its own rhythm. But this observation of Mackenzie is not unique. I have already referred to the case published by Chauveau <sup>(10)</sup> in 1885, which deserves all the closer consideration here because it was studied by him with the greatest accuracy.

In his patient the pulse was continually 21-24 per minute, while the auricles were giving 60-66 beats in the minute. Chauveau says: "Ici les deux organes, oreillete et ventricule, jouaient d'une manière tout à fait indépendante. Chacun semblait travailler pour son compte sans se soucier du travail du voisin, et cela, d'une manière constante, permanente; jamais les deux organes ne s'influençaient réciproquement, si ce n'est quand leurs mouvements coïncidaient dans une de ces recontres fortuites que la discordance régulière des deux rythmes amenait forcément d'une manière périodique."

The cardiograms and pulse tracings which Chauveau gives in proof of this assertion, and his interpretation of them, leave no doubt whatsoever that the auricles and ventricles were really acting independently of one another. Fig. XVII. is a copy of the diagram which Chauveau gave in his paper to illustrate the movements of the heart in his patient; for details, I would refer the reader to his original article, which is well worthy of perusal.

In Fig. XVII. eight auricular contractions occur for three of the ventricle; the independent action of the two chambers is seen at a glance; and just as Mackenzie was able to demonstrate that, in his cases, the two auricles and the two ventricles acted together, Chauveau was able to prove in his case that the two auricles at least acted synchronously.

There is therefore no choice left in this case but to diagnose a

"Stannius's ligature" at the auriculo-ventricular groove. It is quite obvious that this patient was in perpetual danger of his life with such an irregularity of the heart as this, where the ventricle took on its own rhythm permanently and not temporarily, as happened in Mackenzie's case. And Chauveau relates that his patient was on his way home when he suddenly expired. From these two cases conclusions could be arrived at as to the rate of automatic stimulus-production in the ventricle in man, viz., that in both cases it was between a third and a fourth of that at the venous ostia.<sup>1</sup>

§ 36. **The Cause of Heart-Block.**—All these cases that have just been described have been cases of heart-block. What is the cause of it?

After all that has been said, there can be only one answer to those who have followed the results of physiological experiments intelligently, and it is this: It is in all probability through an arrest of the stimulus-conduction at the auriculo-ventricular groove that

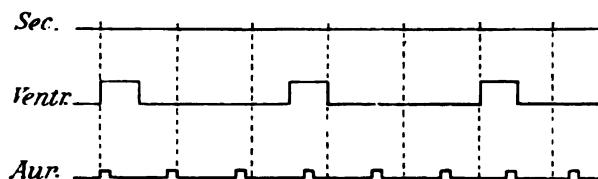


FIG. XVII.

the ventricular systoles drop out, and the auricle and ventricle are ultimately completely separated from one another.

In discussing this question more fully it must certainly be admitted that a great disturbance of excitability, either alone or in conjunction with inhibition of the conduction-power, might also cause ventricular systoles to fall out rhythmically, owing to the fact that the muscular fibres connecting the auricle with the ventricle have so far lost their excitability.

And yet in this case too it is possible that a disturbance of conduction is the most likely cause. In support of this one might point in the first instance to the work of von Kries,<sup>(65)</sup> which was already alluded to. He observed in a case of diminished excitability that either only every second auricular systole, or every fourth, or every eighth was able to produce a contraction of the ventricle, a phenomenon for which he was able to give a full explanation. In our cases we saw that every second, third, and fourth systole of the auricle are followed by one in the ventricle, a condition which

<sup>1</sup> Vide Appendix 3.

in my opinion might also happen with diminished excitability, if a certain portion of the heart-muscle could respond say only to every third stimulus, while the surrounding muscle contracted with every stimulus.

But there are positive proofs of the arrest of conduction in these cases. If we look at the tracing by Mackenzie, Fig. XV. *b*, we see in it a fact, especially pointed out by him, and of decisive importance in the interpretation of this pulse, confirmed as it is by the results of physiology which have already been alluded to. In the venous pulse the first two auricular elevations *a* occur a very little before those of the carotid *c*. This interval represents the time that elapses between the auricular and ventricular systoles, the latter of which produce the carotid pulse. When the ventricular systole comes later after the auricular, the carotid wave will also appear later after *a*. We see now quite clearly that, after the long pauses caused by the falling out of two ventricular beats, the wave *c* follows *a* more quickly than after the shorter pauses that were produced when one ventricular systole dropped out; and this does not result from the too early occurrence of the auricular wave; on the contrary, *a* appears with perfect regularity, and in the latter instance, *c* actually comes in too late. The ventricular beats therefore follow the auricular later after the short pauses than after the long ones. The interval  $A_s - V_s$  however depends solely upon the conductivity of the cardiac muscle; this patient thereby affords the strongest *proof* of the great disturbance of conduction.

The same variation in the interval  $A_s - V_s$  is, if possible, even better exemplified by Mackenzie's second case. In Fig. XVI. *c* there is no *c* after *a* in the first three pauses, no ventricular systole following the auricular. The interval  $a - c$  ( $A_s - V_s$ ) remains constant. When again *c* follows *a* twice in succession, the distance between them at the second beat is much greater.  $\Delta$  has then scarcely recovered itself completely, and so the conduction is delayed.  $V_s$  follows upon  $A_s$  much later, and *c* therefore upon *a*. This very peculiarity which was also pointed out by Mackenzie, and is extremely well marked in Fig. XVI. *d*, proves that in this heart the conduction from auricle to ventricle had been very seriously impaired. This positive fact then is also sufficient to make us regard the arrest of conduction as the cause of the missing of the ventricular systole.

As regards Fig. XVI. *a* the increase of the length of the interval

$A_s$ — $V_s$  can be plainly seen from the increase in the distance between  $a$  and  $c$ , and with the help of the accompanying time-marker it can be directly measured. The interval increases until a ventricular systole ultimately drops out; the auricle, however, goes on beating regularly all the time. In the pause that ensues  $A$  gets time to recover considerably. After the pause  $V_s$  follows  $A_s$  so quickly that in the first systole of the new group the waves  $a$  and  $c$  in the venous pulse run into one another. An especially high wave in the venous pulse then occurs; and Mackenzie explains it on the ground that the auricular and the ventricular contraction take place simultaneously, a condition which he had observed when extrasystoles are found, and had analysed. Since the two chambers contracted simultaneously, the auricle was unable to drive the blood it contained into the ventricle: its contents therefore must all flow back into the jugular vein (*cf.*  $a$  in Fig. XVI.  $a$  and  $b$ ). I would, however, put forward another explanation. One would expect that after the pause  $V_s$  would follow  $A_s$  quickly, because the conduction is so much better. If we measure the tracing accurately, it is found that after every pause  $c$  ( $V_s$ ) appears really a little after  $a$  ( $A_s$ ); in other words, the contractions of the two chambers do not take place simultaneously, but occur in their usual order with a shorter interval between them. The fact that the wave  $a$  in the venous pulse above-mentioned seems to be much higher than one would expect, from the partial overlapping of  $a$  and  $c$ , is explained on the ground that through the dropping out of a ventricular systole the circulation is for the moment at a standstill, and therefore the auricle will contain a greater quantity of blood than usual; hence it is not surprising that the first auricular systole after the pause will send back a much bigger wave into the jugular than it would otherwise do.

This case then agrees in every particular with the explanation of heart-block by a disturbance of conduction.

And I should like, by the way, to draw special attention to the fact that the radial pulse in this case presents exactly the same variations and the same allorhythmia as I described in my first case, and noted as due to a disturbance of conduction. The effect of the interval on the radial pulse is shown here very distinctly. I could scarcely have hoped for a fuller confirmation of the explanation which I then gave.

§ 37. Can we assume that Arrhythmia is ever due to a Disturbance of Conduction?—From an analysis of these cases of

irregularity of the heart, we are led to conclude that they are exactly similar to those forms of allorhythmia that are obtained experimentally as the result of a greatly diminished  $\Delta$ .

We have seen forms of allorhythmia, in which probably the conduction of the entire cardiac muscle has been affected, so that systoles of the auricle as well as of the ventricle drop out periodically. Through the finer details in these cases of allorhythmia it was possible to exclude a disturbance of other functions, and to regard an arrest of conduction as the sole cause, inasmuch as they absolutely correspond with the changes in rhythm that are observed in any portion of cardiac muscle from this cause.

Moreover, we saw that in man only ventricular systoles drop out under certain circumstances, and that, too, in great numbers. The similarity between such a condition and experimental heart-block was very striking; and we are not only led by a comparison of them to think that the cause of it too was a disturbance of conduction, but it was actually proved to be so in Mackenzie's cases.<sup>1</sup>

Before we discuss the importance of this explanation for pathology, and especially for further researches in this direction, we must first turn to a criticism which H. E. Hering<sup>(43)</sup> made on my previous explanations.

It is impossible for me to take up Hering's arguments one by one here, nor do I think any object would be gained by doing so. If I did, I would be bound to take up the discussion of subjects that have no relation to this matter; but his remarks on the possible causes of the dropping out of systoles have no bearing upon the cases which I have analysed, both here and in my previous works, nor does he express anything new in them. The main points in Hering's criticism are: (1) that I have not given any absolute proof of my explanation; and (2) that we have no right to assume that the disturbance of conduction may be the sole and only cause.

In reply to the first point I would say, that it is hardly ever possible to bring forward such absolute proofs as Hering requires; but, on the other hand, there is such an absolute similarity between the forms of allorhythmia that are obtained by experiment and those found in man, that the explanation given here must be accepted until it is proved to be wrong. But now that the variations of the interval  $A_s - V_s$  have been proved with such absolute certainty in Mackenzie's beautiful tracings, and the variations in

<sup>1</sup> *Vide* Appendix 4.

the radial pulse, produced by the varying interval  $A_s - V_s$ , correspond exactly with those I have shown and analysed in my cases, the proof which Hering demands is forthcoming. He has not only not brought forward a counter-proof to refute my explanation, but he has not been able to suggest any other for cases I., II., and III. He certainly says that he has often observed similar irregularities in patients with arterio-sclerosis, but he gives no proof of this assertion, and until this is forthcoming nothing can be said about these observations.

The main point of Hering's second contention rests on the opinion which he repeatedly expressed, that we cannot look upon the various functions of cardiac muscle as separate entities; they must be regarded together as stimulability (*Reaktionsfähigkeit*). From this standpoint he cannot of course admit that arrhythmia is due to the disturbance of one of these functions; this standpoint of Hering's we shall again have occasion to consider in discussing pulsus alternans. His criticism, however, is of no value, because this position which he takes up cannot be reconciled at all with the known facts of physiology, as was fully explained in § 9, and again recently proved by Engelmann in the most conclusive manner.<sup>(28, 29)</sup>

With the explanation which he has given of my fourth case (§ 33) he has been, at least apparently, more successful. When this case is considered by itself, as Hering does, it is calculated to shed some doubt on my method of explanation, because it is not known whether the pulse here was really a slow one accelerated at times, or a quick one at times delayed. At the time I paid most particular attention to this question, and on the strength of the perfect similarity of this case to the other three, I was convinced that it was originally a frequent pulse, in which many systoles fell out. Now Hering at once assumes that the pulse was a slow one, but the rate as he estimates it is not correct. In the regular part of the tracing (Fig. 19, Plate V.) it is 56.6 per minute; in the irregular parts, and according to Hering's calculation, it is 68, but, if the rate is estimated from fifty long periods, it comes to 50.3, and hence one is bound to assume that there is distinct bradycardia. In this condition of bradycardia now the shorter periods, according to Hering, should be caused by extra-systoles, which, seeing that there is no compensatory pause, must have arisen at the venæ cavæ.

We must admit at once that if all these systoles that follow one another more quickly were really extra-systoles from the *venæ cavæ*, the pulse would appear exactly as it does here. But whether we can accept this explanation is a quite different question. On closer consideration it appears to have been put up *pour besoin de la cause*. If any one thinks it can be assumed that extra-systoles occur with such continuous regularity at definite intervals, he must also be able to bring forward cases in which this regularity can be seen; when Hering demands conclusive proof of the cause of this form of allorhythmia, even in spite of its *perfect* likeness to the irregularities produced experimentally, he might well be asked to show by some experimental proof that extra-systoles from the *venæ cavæ* are likely to act in this way. He merely makes the assertion, however, that he has met with cases like this again and again. But that is not enough in questions of science.

Furthermore, it is quite impossible to prove that in *this* case we have to deal with extra-systoles from the *venæ cavæ*. As was fully discussed in § 25, and shall again be shown (in §§ 66, &c., and 77-83), it is impossible to determine in man whether the systoles in question are extra-systoles or premature normal contractions whenever they start at the normal point of origin, because the compensatory pause is wanting, and the mechanism of the systoles is a normal one. As was explained before, the occurrence of such at irregular periods in the diastole, or the appearance of extra-systoles at other places in the heart, might then give a clue to the extraneous character of the systoles. But in this case the regular rhythm and absolutely normal character of the systoles is at once noticeable, and there is absolutely no sign of extra-systoles elsewhere.

I presume, however, that any one that looks at such figures as 18 *a, d, e, f, g* will hardly be inclined to say there are extra-systoles there, although in Fig. 18 *b* and *c* the last beat of a group is somewhat smaller.

Hering's explanation then is not founded on a single fact, and as yet must be regarded as being absolutely without foundation. If my explanation, even with the support of Mackenzie's case, is not accepted, it is more in accord with physiological facts, and more justifiable, to attribute the continuous quicker succession of systoles to a variation of the excitability, or the stimulus-production, or a combination of the two, *i.e.* to chronotropic and bathmotropic effects. It is difficult to see by what means the

variations in this case could be produced. It must be remembered that I observed these changes of rhythm in this patient for several years. Of course variations like these occur from the influence of respiration on the pulse rhythm (*cf.* § 58). The variable size of the slow and quick periods, however, as well as the absolute length of the periodic variation, shows that there are no variations due to respiration here. We shall return again to this as a possible explanation (*cf.* § 58).

Before I leave Hering's criticism there are two statements of his which I cannot pass over in silence. They are found on page 5 of his work, to which we referred above.

I had previously observed that in my last case the disturbance of conduction might perhaps be caused by the high frequency which must be assumed if my explanation of the case is correct. Hering then says, giving the passage in italics as one of special importance: "Supposing that this theory of Wenckebach were correct, the abnormally high stimulus-frequency would be the cause of the bradycardia, and not the diminution of the conductivity."

What Hering really means by this I do not understand. If my theory is correct, the high frequency is the cause of the diminution of the conductivity, and it is just the arrest of conduction that converts the high frequency into bradycardia, *quod erat demonstrandum*.

The second statement of Hering contains an even worse argument, for it gives a totally wrong idea of the question. He says: "In order to show the style of argument that is adopted it will be enough to point out the way in which Wenckebach quite unconsciously reasons in a circle. He calculates the great number of contraction-stimuli by supposing that all the long periods are intermissions. That all the long periods are intermissions he explains by supposing that the conductivity of the cardiac muscle is diminished. That the conductivity is diminished he explains on the supposition that a large number of contraction-stimuli is present."

Hering has certainly pointed out very plainly how to reason in a circle, but the circle is completed by a wrong conclusion. The question as to the possible effect of the high frequency on the conduction-power has nothing to do with my line of proof, and was mentioned at the very end of my article.<sup>(120)</sup> I have then, as

now, sought the proof of the diminution of conduction solely in the complete analogy between the forms of allorhythmia that were most frequent in this patient and those forms in my other cases, which very strong reasons compelled us to attribute to arrest of conduction, and which Hering could not otherwise explain. This mode of argument he simply overlooks; he makes the mistake of discussing this case apart from the rest, and rejecting these points of similarity between them.

Hering's view, therefore, will not in my opinion make any difference in the explanation of this form of allorhythmia, especially since recent facts have shown beyond all doubt that it is possible for every alternate systole to fall out. It has long been known that systoles drop out, or apparently do so, in many other ways, and this fact was previously made use of by me <sup>(123)</sup> in explaining the nerve influences on the heart, and will be discussed fully later on. Hering's remarks on this point in the same article are not calculated to open up new lines of analysis of cardiac irregularities. His arguments are based on the theory from which he starts; he sums up the various functions of cardiac muscle (and it is just by the sharp differentiation of these that we can obtain an insight into the physiology and pathology of the heart) under the one collective term *stimulability*, and in the same way classes all the various irregularities, for which he can assume a myogenic origin, as "*myoerethic*" (*myoerethische*) irregularities. How unsuitable this term is for the further study of the various types of arhythmia is seen not only in this article of his but still more in his paper on "*Pulsus Pseudo-Alternans*," which must be dealt with in more detail in the chapter on disturbances of contractility.

§ 38. **The Importance of the Disturbance of Conduction in Practice.**—The theory that a disturbance of conduction can give rise to a definite form of allorhythmia, and that conclusions can be drawn from this allorhythmia, which is distinguished by certain characteristics, about a disturbance of conduction, is of very great importance in clinical work. Yet a large number of questions will have to be solved before any deductions as to diagnosis or indications for treatment can be drawn from this condition with certainty. Still, if this goal is to be aimed at, it is absolutely necessary to make a careful analysis of the various types of allorhythmia and arhythmia, and obtain in this way a larger

amount of material to enable us to form an opinion on this matter. Moreover, there are still many physiological and pharmacological facts that must be elucidated before the results of the analysis of the pulse can have full practical value. At the same time, no one can deny the considerable value of our present knowledge of the irregularities of the heart.

In the first place, we must ask ourselves under what conditions disturbance of conduction can occur in experiment, and then inquire if these conditions can be found in man, and especially in the cases before us. Disturbances of conduction are very easily demonstrated in the frog's heart, and most distinctly in a heart that is slowly dying but still continues to live for days, where the diminution of conduction can be followed step by step. A deficient supply of oxygen diminishes  $\Lambda$ , but when it is supplied again  $\Lambda$  increases; the work performed by the heart has also a great effect upon its conductivity. There are few facts known as regards the mammalian heart. Hering says (<sup>48</sup>, p. 12) that in the mammalian heart it requires a relatively strong stimulus to produce disturbances of conduction. But what these "relatively" strong stimuli are, I cannot find stated anywhere. The first question that requires solution is this:—

*What conditions can produce disturbances of conduction in the frog's and the mammalian heart?*

I would specially refer to the conditions that can readily be imagined in the case of the human heart: bad nutrition, brought on by constitutional diseases, or by local anæmia due to diseases of the vessels, abnormal composition of the blood, toxic conditions, and infectious diseases; degeneration of the cardiac muscle, particularly at the auriculo-ventricular groove, chronic fibrous myocarditis, &c. It is natural to suppose that disturbances of conduction can also be observed in the *dying* human heart; this was pointed out by Belski,<sup>(4)</sup> and is exemplified in my second case and in that of Chauveau. It can also be inferred with very great probability from physiological facts that fatigue of the heart may very soon show itself in disturbances of conduction, and this can also be seen in man, as in my first and third cases, through the effect of physical exertion on the allorhythmia. Experiments, such as those which Loeb, Overton, Göthlin, and others have made on the effect of certain ions on the heart's action, seem most likely to yield valuable information with regard to the nature of stimulus-conduction and

its disturbances. Experiments on these lines are at all events necessary for the development of the clinical aspect of the question.

We know, moreover, that the conduction can be greatly altered by the action of the nerves, particularly through the vagus. In recent years our knowledge of the action of the vagus has been greatly increased by the experiments of Muskens, Engelmann, and others. It is now known that the vagus can produce dromotropic as well as inotropic and chronotropic effects. With regard to the cases under consideration, therefore, the question arises :—

*Is the disturbance of conduction the result of nerve influence or of injurious influences arising in the cardiac muscle?*

This question must be answered for each case by itself. The signs of arrhythmia that arise from nerve influence will be dealt with in a special chapter later on; we need only observe here that the cause of a continual and constant arrest of conduction, such as we find in my first, third, and fourth cases, as well as in that of Mackenzie, must be looked for in changes in the heart itself rather than in any nerve influence. On the other hand, in cases where the disturbance appears in paroxysms and is accompanied by distinct nervous symptoms, as frequently occurs in Adams-Stokes' disease, one might then think of some nerve influence. The cautious administration of atropine may be useful in some cases for the further investigation of this problem.

In looking for causes of disturbances of conduction we must not overlook the secondary dromotropic effects of other disturbances. Thus a high frequency, which does not give  $\Lambda$  time to recover itself, might, as I have pointed out before, very readily cause a disturbance of conduction in man as it does in experiments on animals. And in this connection it is a remarkable fact that a fairly high frequency is present in many cases, as in my third one, and also in the cases of heart-block at the auriculo-ventricular groove. Hering says, it is true, that the contraction is delayed by applying stimuli in experiments (as in the dying heart), but adduces no proof for his assertion that these phenomena must therefore invariably go together. If there is a high frequency that alone may cause disturbances of conduction. And when the injurious consequences to the preservation of the heart's action that may follow a continued high frequency are added, it seems to us to be a most favourable thing for the heart that many systoles do fall out from an arrest of the conduction; and we can understand that

the heart can act much longer with this falling out of beats and the rest that is thereby given to it than would be possible without it. And we must not forget the important part which, as Engelmann so conclusively proved (*cf.* § 11), is taken by the conductivity in the "myogenic self-regulation" of the heart.

When the importance of a solution to these questions is at once apparent, it is hardly necessary to discuss at any length how our knowledge of disturbances of conduction will only acquire some practical importance when we know *what are the extrinsic and intrinsic conditions, and particularly what are the drugs, that have a beneficial effect on conduction.*

The fact that this question is an urgent one shows how much the chapter on the pharmacology of the heart requires to be rewritten. And this is above all necessary for digitalis, the most studied of all our potent drugs. The action of medicinal doses of digitalis on the various functions of cardiac muscle, with and without the presence of nerve influences, is a subject that still requires investigation. Seeing that digitalis is of so great value as a cardiac tonic, such an inquiry, together with its application to the treatment of heart disease, would be of the highest importance. Herein, too, lies the significance of analysing the arhythmia as we have done here. If, as I have endeavoured to prove, it is possible to diagnose a considerable disturbance of conduction (and this holds good of the other functions of the heart as well), we shall be able, with the help of the knowledge of cardiac poisons that is still to be obtained, to determine the indication or contra-indication of any particular drug with considerable certainty. In my first communication on this subject I made the assertion that digitalis is contra-indicated in disturbances of conduction because in big doses it stimulates the vagus, and stimulation of the vagus can diminish the conduction. By this somewhat sweeping assertion I sought to direct the attention of physicians to the importance of analysing irregularities of the heart, and I find from the literature that this object has been attained. This statement is borne out by clinical and physiological experience; whether it is absolutely correct or not can only be decided when a large number of experiments have been made in this direction; the subject is, however, not yet ripe for full discussion. Hering has discussed the matter fully (<sup>43</sup> p. 20, &c.). All who have read the more recent literature on the action of the vagus by Muskens, Engelmann, Hoffmann, and others, will be con-

vinced that even this description is only fragmentary, that there are many factors to be taken into account, and that contributions of any value to this question can only be obtained from experiments that are fully recorded.

I trust, however, that what I have said here is sufficient to show the importance of the subject, and to indicate problems that have still to be solved.

#### THE DISTURBANCES OF CONTRACTILITY

§ 39. **The Disturbances of Contractility.**—The results of physiological experiments in recent years show that the most important function inherent in the cardiac muscle, contractility, can be altered to a considerable degree by influences of various kinds, such as water, poisons, and through the nerves. This alteration can occur independently of the other functions, and may be positive as well as negative. The contractility is measured by the size of the contraction, and this can be done with very great accuracy, because the heart reacts to every effective stimulus with all the power of contraction of which it is at that moment capable. The changes in this function are shown by the size of the contraction not only in experiments but in the human heart. But it is a question whether in man changes in the size of the contraction can really be attributed to variations of contractility, for this function is subject to secondary influences, and especially to those arising from the systole. Every systole paralyses the heart, and during the diastole the contractility is restored with more or less rapidity in the same way as has been proved for the other properties of the heart; the contractility is therefore largely dependent on the length of the pause after a contraction.

I have already endeavoured to show that it is probable that greatly diminished contractility in man can actually be demonstrated by a definite form of allorhythmia<sup>(122)</sup>: it is the "pulsus alternans," the typical allorhythmia due to a disturbance of contractility, the reverse of the regular intermission, which we found was due to an impairment of conduction-power. The alternating pulse consists in the alternation of large and small beats in the radial pulse; but to understand this allorhythmia properly it will be necessary in the first place to discuss the physiological facts that can throw some light on this matter.

§ 40. **Alternating Action of the Heart in Experiment.**—The size of the contraction, as we remarked already, is an exact and direct measurable standard of the entire contractility of which the heart is capable at the moment of stimulation. We must, of course, bear in mind that the size of the contraction of *the entire heart* can be influenced by other factors, *e.g.* through the unequal distribution of a disturbance of excitability and conductivity, certain portions of the heart are unable to contract, and hence the contraction as a whole may appear small or at least modified. Muskens <sup>(82, 83)</sup> has made a special study of the disturbances of conduction in this direction, and he asserts that, in consequence of a disturbance of conduction in one portion of the heart, the contraction might be reduced in size, because all the muscular fibres did not contract. He has, in fact, attributed all the differences in the size of contractions to this influence, and accordingly would represent conductivity as the primary function of cardiac muscle. This view of Muskens is, however, purely hypothetical, and has been finally refuted by Engelmann. <sup>(26, 27)</sup> In certain cases, however, disturbances of conduction can have a secondary inotropic effect, and this is an established fact with which we will have to reckon.

If we suppose that the muscle of the living heart gradually loses its contractility, while the stimulus-production, excitability, and conductivity remain constant—a supposition which we may now make—we shall see that the contraction continually diminishes in size. But when the contractility has been reduced to a certain extent in experiment, it is found that an alternation of large and small beats appears for a longer or shorter period. This alternation of the heart was described and illustrated by Engelmann in 1897 (<sup>20</sup> Plate II., Fig. 1), as well as by others. The contractility can also be artificially reduced by stimulating the heart into very rapid contraction; the contractility has then little opportunity to recover itself; it will be sooner impaired than with a less frequency. Under these circumstances Engelmann observed the alternation appear on raising the frequency of stimulation, and disappear again on diminishing it. F. B. Hoffmann, who made an elaborate study of this subject, <sup>(57)</sup> brought about the reduction of the contractility by stimulation of the vagus, which produced a “hypodynamic condition” in the heart. Under these conditions, Hoffmann also observed an alternation of the heart.

A few years ago Hoffmann explained why there is such an alternation of large and small beats when the contractility is much impaired. From the older and more recent researches of Engelmann (<sup>26</sup> p. 105), O. Frank,<sup>(32)</sup> and the work of F. B. Hoffmann above mentioned, it is found that, when the contractility is lowered, the contraction is made more quickly than the normal one, *i.e.* it does not last so long, and this is quite independent of the manner in which the contractility of the heart was reduced (say, by high frequency or by stimulation of the vagus). In this condition both systole and diastole are shorter; the cardiac muscle sooner reaches the maximum of its contraction, and sooner returns into a position of rest. Hence the pauses between each pair of beats are longer. If now one period becomes a very little longer from some cause or other (by changing the frequency once, for example, as in Hoffmann's experiments), the next systole will be a little larger by reason of the longer rest which the heart obtained. But, on account of the greater length of this big contraction, it will be followed by a somewhat shorter pause, even if the heart returns again to its normal rhythm at once. The next systole will therefore be smaller; but as it lasts a shorter time, it is followed again by a longer pause, and the succeeding systole will again be larger: this experiment cannot be repeated for a considerable time, but it is proved conclusively by Hoffmann's experiments that this actually occurs.<sup>1</sup>

When such a long-continued alternation of the heart can arise by just changing the frequency once, solely through the influence of the alternating length of the pauses, it is quite conceivable that a similar condition might also arise in man from a disturbance of contractility; for the slight differences in the period-lengths that favour its occurrence are always present. But before we turn to the application of this knowledge to human pathology, we would here make mention of some physiological facts.

Among some old tracings of Engelmann I found a very

<sup>1</sup> In a recent article, W. Trendelenburg (<sup>114</sup>) confirms the shortening of the period of contraction from negative inotropic influence, and indeed asserts: "While the inotropic effect was compensated for by simultaneous chronotropic influences on stimulation of the vagus, while, in other words, the height of the contractions remained constant, the duration of the contraction was reduced during the vagus stimulation by  $\frac{1}{10}$ " in one case and  $\frac{1}{8}$ " in another. Even with a pure arrest of contractility, we can see in the auricle that, after a short stimulation of the vagus, a contraction has again reached its former height, but the period of contraction is still shorter than it was before the vagus was stimulated. This points to the conclusion that shortening of the period of contraction is an essential part of the arrest of contractility, and does not appear to be merely secondarily connected with the diminution in the height of the contraction."

instructive example of the alternating action of the ventricle in a frog's heart. Fig. 21, Plate V., is taken from this tracing.<sup>1</sup> When we look at it closely, we see that the interval  $A_s - V_s$  ( $= 17.5$ ) keeps perfectly constant, and therefore there is no variation in the rate of conduction. In the second place, we see that the rhythm, even of the unequal ventricular contractions, remains the same (the ventricular period  $= 45$ ); and further, we find that the top of the contraction-wave is much sooner reached in the small systoles than in the large. In this way a considerable difference in the length of the pauses after large and small systoles in the manner mentioned is observed with simple alternation of the ventricle and the rhythmical commencement of each contraction; from the longer duration of the large systole the pause between the top of it and the beginning of the small one is nearly  $= 18$ , while the pause following the small one is  $= 24$ . The proportion of the one to the other is therefore  $= 3 : 4$ .

The very remarkable experiments which W. Straub<sup>(100)</sup> made with antiar on the action of the frog's heart show the development of a half-frequency with gradual diminution in the size of the contraction. But this half-frequency is not reached until an alternation of large and small beats has been going on for some time. If a sufficiently small dose was administered it was possible to make this stage of alternation continue, but if a bigger dose was given the smaller systole then rapidly and regularly diminished in size and ultimately disappeared entirely. The reduction in the size of the contraction and this interesting transition stage show very clearly that in addition to other disturbances which were thoroughly investigated by Straub, the contractility was also reduced. Straub expresses it in this way: "Antiar poisoning has an inhibitory action on the process of the rhythmical production of the potential energy in the cardiac muscle," and "Prolongation of the refractory phase leads to a diminution in the height of the contraction." That is equivalent to saying that the contractility is no longer restored so quickly and completely as normally. Disturbances of other functions also arise; the excitability no longer recovers so thoroughly, but that does not reduce the size of the systole, because as long as the stimulus produces a contraction, that contraction is a maximal one; it is either a maximal one, or there is none at all; if then the contractility were not impaired, the systole would rise to its normal height. The

<sup>1</sup> The numbers are expressed in  $\frac{1}{100}$  seconds.

conductivity, which was also very carefully studied by Straub in this case, exhibits different changes under the action of this drug, as we saw in the last section, and shall discuss afterwards more fully (§ 42). The rhythmical stimulus-production also remained unimpaired, as Straub points out, for it would be otherwise impossible to explain how the frequency was reduced by so many times the normal rate. From the great number of symptoms, therefore, we are bound to attribute the signs of diminution in the height of the contraction wave, the alternation, and the gradual reduction and eventual disappearance of the small beat to a disturbance of contractility. This furnishes us with very important facts for the analysis of irregularities of the heart in man. We shall return again to Straub's experiment and to the work of Rümke on this subject.

In the mammalian heart a similar alternation of large and small beats is observed from the action of certain poisons. I would refer for example to the work of Rümke <sup>(100)</sup> and to that of Magnus <sup>(7)</sup> on sending gases through the heart. In Fig. 5 of Magnus' work we see alternating action of the heart, while Fig. 7 shows the most beautiful transition through the uniform diminution in the size of every second systole down to half-frequency.

In a recently-published paper O. Langendorff <sup>(98)</sup> has demonstrated the injurious effect of hæmolytic blood on the heart. When the action of the heart is very much deranged it is very remarkable that a long-continued alternation of the amplitude of contraction sets in. It is most probable that the contractility of the heart is then particularly affected. The injurious substance appears to be the potash that is normally locked up in the blood corpuscles;  $\text{Ca Cl}_2$  can then restore the "power" or contractility of the heart.

Finally, we must refer to Göthlin's experiments <sup>(37)</sup>; Fig. 5 A and 5 B in his paper show alternating action of the heart, passing into half-frequency.

If now the question is asked whether there is any affection in the human heart similar to this alternation, it must most distinctly be answered in the affirmative. Yet we shall see that alternation in man occurs in two distinct forms that can be easily interpreted.

§ 41. **Alternating Action of the Heart in Man.**—Pulsus alternans has been long talked about in the pathology of the heart. Indeed it is a very much disputed question whether there is real alternation of the heart, or whether this phenomenon must be attributed to so-called bigeminy or to pulsus bigeminus. After

Traube<sup>(112)</sup> had first described an alternating pulse, Fraentzel,<sup>(32)</sup> Sommerbrodt,<sup>(104)</sup> Riegel,<sup>(92, 94)</sup> Schreiber,<sup>(102)</sup> Dehio,<sup>(16)</sup> and many others supported and opposed the view that *pulsus bigeminus* and *pulsus alternans* were identical. This controversy, however, is now of very little interest, because the causes of the various forms of arhythmia, which frequently exhibit a strong resemblance to each other, were at that time entirely unknown. As I have expressly stated before,<sup>(122)</sup> the point is to decide whether in any concrete example the case was one of alternation of the heart or of extra-systoles, the usual cause of so-called bigeminus. This is the form in which the question must now be put for solution, since H. E. Hering<sup>(44)</sup> denied the existence of *alternans* in man, and will only admit of a "*Pulsus pseudo-alternans*" produced by extra-systoles.

When the contractility of a heart is very much impaired, not for a short time by some nerve influence (*cf.* § 59), but through some continuous or even constant cause, an alternation of large and small beats will appear, not from time to time, but go on almost continuously, because, as we pointed out before, very small changes in frequency, capable of keeping up the alternation, are always present. If we take this as the test of real alternation, it is easy to exclude at once most of the cases that have been recorded. On looking through the literature it is remarkable that those observers who met with a real *alternans*, and they are very few, were all surprised at the long-continued occurrence of the phenomenon. The astonishing regularity of its appearance is perhaps the best sign to draw the doctor's attention to the fact that he is dealing with a special form of allorhythmia, and not with extra-systoles. Of the cases found in literature I would here mention those of Fraentzel, Sommerbrodt, Schreiber, and Dehio, in which the continuance of the alternation was very striking.

I have as yet observed only two cases of real alternation myself, and one of these I have already described. The first case was that of a man seventy years of age, who had suffered from a severe attack of influenza, and subsequently complained of fatigue and shortness of breath on the slightest exertion; he had arteriosclerosis, but no sign of any valvular lesion. This patient had a regular *pulsus alternans* for weeks at a time, during which the beats became equal only now and then for a few moments. Pulse tracings taken from him are reproduced here at greater length than they were in my former paper, in Fig. 22, *a, b, c*, Plate V.

When these figures are carefully studied, the first thing that strikes one is the great regularity of the alternation; as we said, it continued for weeks in this patient. In the second place, it turns out that the small pulse-wave appears always a very little too soon. This agrees with the fact that on auscultating the heart the sounds of the small beats appear to come a little too early. They are, however, normal in character, but just slightly weaker than the big beats.

This condition might lead one to take this pulse for a bigeminus, and to think that extra-systoles regularly occurred. I have already shown<sup>(122)</sup> that this explanation must be here rejected, and yet H. E. Hering<sup>(44)</sup> has asserted, although he has not attempted to adduce any proof, that this arrhythmia was produced by extra-systoles; but I can demonstrate to the contrary, (1) that it is quite impossible to explain this pulse on the theory of extra-systoles; (2) there is a perfect agreement between this alternation and that obtained experimentally.

As to (1) I must point out that, as auscultation shows, the weaker beats seem to come a *very* little too early, they present a perfectly normal character on auscultation, and, if they were extra-systoles, would have been bound to show a larger pulse-wave just because they occur so late in the diastole. Moreover, extra-systoles have never been observed to occur regularly for many weeks at a time, not merely after every second beat, but invariably in exactly the same phase of the cardiac cycle. And even in cases where extra-systoles did occur for a considerable time, this regularity always alternated with normal parts, or parts showing much greater disturbances of rhythm. When we look up the literature on this point we find this always mentioned. Among recent writers I will only quote Lommel<sup>(72)</sup> and Mackenzie.<sup>(75)</sup> All the other characteristics of extra-systoles are absent. And finally, the theory of extra-systoles would not be able to explain the short intervals of regular movement and its gradations into the alternating action, as will be explained more fully later on.

As to (2) we can quite easily understand this alternation going on for weeks, if we assume that there was a disturbance of contractility. In the last paragraph we saw how an alternation is developed under these circumstances and under the influence of minute variations of rhythm. If we look at Hoffmann's figures, and especially at the tracing given here in Fig. 21, it is clear that auscultation must reveal exactly the same condition in alternation of the heart

as it did in this patient. The second cardiac sound occurs at the end of the systole, and we have seen that just as the top of the small beat is reached, and *the second sound thereby heard much sooner, although the systole begins with perfect regularity*, as in Fig. 21, so the pause that is heard on auscultation is much longer after the low beats than after the high. If one could have auscultated the heart in the case of Fig. 21, the smaller beat would have been distinctly heard occurring prematurely. When, therefore, Hering (*loc. cit.*) asserts that the premature appearance of the weaker systoles which could be proved by auscultation does not agree with my explanation, and thinks that I should have held by the results of auscultation, he is most decidedly wrong. The results of auscultation really bear out my explanation, and oppose the idea that the condition is due to extra-systoles.

The case is somewhat different with the small pulse-waves and their slightly premature appearance, because we have seen that in an alternation of high and low beats *the beginning of the systole* appears at perfectly regular intervals. Should we not then expect that *the beginning of the pulse-wave* in the radial artery also appears at equal intervals? In my previous paper I expressed the opinion that a small pulse-wave might possibly be transmitted through the artery with greater rapidity than a large one, or that a small systole might pass along more quickly than a larger one. Here again Hering has taken strong objection to these hypotheses, while some doubt has been cast on the former by others as well. As regards the theory that the small blood-wave is transmitted with greater rapidity, I have asked the opinion of the physicist Dr. Hoorweg, of Utrecht, on this question, which is a purely physical one. He carried out a large series of experiments on the movement of the blood in the arteries, and was kind enough to write to me as follows: "It must be assumed that a small wave is, generally speaking, transmitted more rapidly than a large one for the following two reasons: If we take into consideration the elasticity of the vessel wall, and the friction of the fluid particles on one another, as Korteweg<sup>1</sup> does, we get a formula which shows that short waves have a greater speed of transmission than long. If no other influences came into play, then the premature occurrence of the small waves must be the rule, an assertion which I believed I was right in making. But there are other factors at work. The simple formula

<sup>1</sup> D. J. Korteweg, "Over voortplantingssnelheid van golven in elastische buizen." Acad. Dissert., Amsterdam, 1878.

of Young for the rapidity of transmission ( $V$ ), without taking into account other influences, is  $V = \sqrt{\frac{Ea}{2R\rho}}$ , where  $E$  = elasticity of the vessel wall,  $a$  = thickness of its wall,  $R$  = radius of the artery, and  $\rho$  = specific gravity of the blood. From this formula it follows that when  $E$  remains constant,  $V$  becomes greater as the blood-pressure is reduced ( $a$  being then greater and  $R$  less). Various factors have an effect upon the transmission of the wave, and for the first reason a greater effect on small waves than on large. We cannot, therefore, at once assert that the propagation of the small wave must *always* be more rapid, as I had erroneously done, but that it is so in most cases."

There is, however, another important influence on the rapidity of propagation, viz., the speed with which the ventricle empties itself, because it controls the steepness of the wave as well as the sinking of it. The rapidity with which the ventricle empties itself depends again on the rapidity of contraction, while it is dependent on the conductivity of the cardiac muscle. This influence will, however, be discussed again in speaking of other forms of alternating pulse.

When it follows, from what has been said, that the form of the pulse, as well as the results of auscultation, correspond exactly with the alternation obtained experimentally, this explanation becomes a most probable one by reason of peculiarities in these pulse tracings which I have already laid stress on, but which have been passed over by Hering in his criticism.

We have seen that in a disturbance of contractility, small variations in the period, which are always present in man, keep up the alternation, which might gradually adjust itself if the periods were always absolutely equal. But while the variations can do this, they can also abolish the alternans for a short time. The parts of the sphygmogram showing this short regularity were reproduced in my former paper, and I suspect that they have failed to convey an impression of the extraordinary regularity of the alternation, although they have perhaps led Hering to put forward a false explanation. I have therefore given a longer portion of the pulse tracing in this book (Fig. 22 *a*). If it is carefully examined, it will be found, in the first place, that there are small variations of the period, but, generally speaking, the difference in length between the longer and shorter periods is  $1-1\frac{1}{2}$  twenty-fifths of a

second, the period of the small wave is .02"—.0265", and so this wave appears a very small degree too soon. At the end of the tracing now the following interesting condition is seen: The period, marked (1), happens to be shorter than the normal; hence that systole follows the preceding weak one sooner than normally. The contractility has not been restored so completely as usual, hence the systole is smaller and does not last so long; the next systole (2) is therefore greater than would otherwise be the case, then a slightly longer pause follows, the systole is again larger (3), and the result is that the alternation returns again and goes on as before. A similar example is given in Fig. 22 *b*. There we find that the wave (1) comes sooner after the preceding wave than could be expected; so that contraction occurred at a time when the contractility was not yet fully restored, and therefore cannot be looked upon as a big pulse. There follows now a somewhat longer pause, and after it a systole not very small, but one of medium size (2). A short pause now appears again, and after it a very small beat, and so the alternation is again restored. In Fig. 22 *c*, in which, unfortunately, the time-marker did not record itself, seven regular beats of medium size with slight variations occurred in succession, after which the alternating action is again resumed. In this figure, too, we can distinctly see the transition from the non-alternating to the alternating stage by the continual diminution of the pulse-waves, 1, 2, 3, 4, and 5, in exactly the same manner as we see it in experiments (*cf.* § 40). These small regular portions, which it is absolutely impossible to explain on the assumption that they are extra-systoles (who could tell what are extra-systoles here?), afford very strong evidence in support of the theory that a great disturbance of contractility is the cause of the alternation.

It is hardly necessary to emphasise the fact that the small pulse-wave can become so small that it is no longer possible to feel it at the radial, or record it. This occurred now and then in this case (*cf.* <sup>122</sup> Fig. 2). I have never yet observed in a regular pulse tracing that this weaker systole can ultimately disappear in man, but still we cannot say it is impossible (*cf.* §§ 59, 74).

As this patient recovered the alternating pulse ultimately disappeared. But, as bearing out the explanation which we have given, the alternation could be set up again for a long time after by any physical exertion, commencing with great exhaustion and

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increased frequency of the heart. I once took a tracing of such an alternation as this, which lasted for half-an-hour, and found the same condition again except that the pulse-waves were bigger and the periods slightly longer (*cf.* <sup>122</sup> Fig. 4). In this case too, where the pulse was apparently much more like a *pulsus bigeminus*, there was no sign of extra-systoles. The condition found on auscultation was the same as in the previous case.

Another similar case, that of a man eighty-one years of age, is shown in Fig. 23, Plate V. The alternation in it is not so marked, but still is quite distinct. The premature occurrence of the pulse-wave can also be observed. It is even less possible to think of extra-systoles in this tracing than in the others: moreover, the alternation was observed to continue for weeks, and now and then disappeared for a short time.

§ 42. *Pulsus Alternans with delayed small Wave.*—The first description of a case of *pulsus alternans* was given by Ludwig Traube, but it differed in character from the type of alternation which we have here described and explained. In the pulse, which he described as a variety of *pulsus bigeminus*, "there is a succession of high and low beats in such a way that one high pulse is regularly followed by a low one, and this low beat is separated from the next high one by a shorter pause than that which separated it from the preceding high pulse." (<sup>152</sup>) Other cases that are recorded show the same phenomenon; to these we shall refer more fully again. The question arises whether there was a real alternation of the heart in these cases, and whether they should be put down as due to a disturbance of contractility. In my previous paper (<sup>122</sup>) I put forward the suggestion that perhaps there was a disturbance of conductivity as well as of contractility in Traube's case, but expressed no further opinion on the matter. Now I am able to say with great probability that a disturbance of conduction has also something to do with this phenomenon.

We have seen that when it is a pure case of impaired contractility the pause after the small beats is longer than after the large; and that in such cases it is only the disturbance of contractility that causes the alternation. We saw that the stimulus-production continues the same, and that a variation in excitability cannot be the cause of this condition, because every effective stimulus, weak or strong, always calls forth the full contraction-power of the heart. We must also exclude a disturbance of

conductivity as the cause of the alternans; still we must take up this point more fully here.

We saw in the last section the forms of allorhythmia that the disturbance of conduction gives rise to; these do not include pulsus alternans. If we look at Fig. 10 *a* and *b*, we see that the height of the contractions certainly varies a little with the length of the preceding period, and yet the contractility of the ventricle appears in no way impaired at the moment when, owing to the exhaustion of the conductivity, the next stimulus is not conducted and the next systole therefore is missed. Whether the contraction takes a little longer time in consequence of the diminished conductivity does not affect the height of it. On the other hand, and in proof, we may remark, of the independence of the two functions, Fig. 22 shows a beautiful example of alternation of the ventricle *without the slightest variation in the rapidity of conduction*. The interval of  $A_s-V_s$ , which always shows the disturbance of conduction best, is exactly the same in length for high as well as low beats. For this reason, therefore, and quite apart from the fundamental question discussed in § 37, we cannot hold that the alternation is due to a disturbance of conduction, as Muskens<sup>(84)</sup> declared recently in all seriousness. But this does not exclude the possibility of a disturbance of both functions occurring at the same time, and it is interesting now to see what will be the result if this does occur. The tracings given by Muskens, although they are very short, offer good examples for this purpose, although we cannot agree with the explanation which he gives of them, for the above reasons. When we make a careful measurement of his tracings, Figs. 7-10,<sup>(84)</sup> we find, as Muskens himself notes, that the interval  $A_s-V_s$  is shorter in the large beats than in the small. He infers from this that the impaired conduction during the small systoles is also the cause of these small contractions, an inference which, for reasons given above, cannot be made. On the contrary, the proper inference to make in this case is that the conductivity has suffered as well as the contractility, and that after the big systole both these functions recover with less rapidity than after the small beats, and hence the systoles which follow the large ones are not only smaller, but the interval  $A_s-V_s$  is also longer. If, however, we measure the systoles in his Fig. 7, from the top of one to that of another, we now find that the top of the small wave is separated from the preceding beat by a slightly longer pause than from the following one, *i.e.* the reverse condition

to what occurs when the conduction is unimpaired. This reverse condition, perhaps, together with the very much slower rise of the small beat, must cause a delay of the small pulse-wave in the periphery.

We see therefore that there is no fundamental difference between pulsus alternans with an early occurring and with a delayed small beat, but that the early or late occurrence of these small beats depends on the state of the conductivity. It cannot be doubted that very small differences in rhythm, and perhaps the various factors in the formula mentioned in § 41, for example, the conditions in the circulation, also play a part, and this explains why the position of the small pulse-wave in some of the cases recorded is not always exactly the same. Before I begin to discuss the cases found in literature, I must here mention the view of Rümke<sup>(100)</sup> which entirely agrees with mine. From experiments which he made on the effect of antiar on the mammalian heart, he too expressed the opinion that pulsus alternans is due to a diminution of the contractility, while the delay of the small beat must in most cases be attributed to an arrest of conduction. At the same time he raises the question, whether the delay in most of the cases of alternans that have been described in man might not possibly be due to the administration of digitalis in those patients, because digitalis can arrest the conduction. Rümke did not bring forward any proof of this suggestion, but it is important that the suggestion was at least made. We must, however, keep firm in our minds that while disturbances of other functions may be present, the pulsus alternans is the result of a disturbance of contractility; or, to put it in other words, even if other functions are affected, no other alternating action of the heart can arise without a disturbance of contractility.

H. E. Hering explains this delay of the small pulse-waves on the ground that it frequently occurs with extra-systoles, in which case it must be attributed to a longer "presphygmie interval" (*Anspannungszeit*) of the ventricular systole. I cannot judge of the correctness of this explanation, as Hering merely states it but does not illustrate it by examples, but I think the simplest explanation is found in a delay of conduction which must necessarily be present when the extra-systole occurs early in the diastole. Such a delay is well known, and can be observed in almost every tracing that shows premature beats or extra-systoles (*cf.* Fig. 5, Plate II.; Systoles 3, 9, and others). Hering will not, however, accept this prolongation of the "presphygmie interval" in explanation of the

delay of the systole itself, which he states he has observed, but assumes that the writing-lever was more slowly raised (in other words, it is an experimental error), or the conduction is delayed. That this latter explanation is the most obvious one is borne out by the facts which we have just discussed, and especially by the figures of Muskens above mentioned. I have briefly referred to this point because it is Hering himself who regards it as possible.

Still Hering will not accept this explanation for Traube's case of *pulsus alternans*, and says on this point: "If we consider, on the one hand, the circumstances (asphyxia, poisoning) in which this form of alternation was elicited experimentally, and on the other those in which the *pulsus alternans* occurred in Traube's patient, we are bound to say that for the present it is more probable that Traube's tracing is one of *pulsus pseudo-alternans*. Clinical observations, however, must be left to decide the matter."<sup>1</sup> Now, clinical facts have so conclusively demonstrated extraordinary disturbances of the various cardiac functions, contractility included, that no weight whatsoever can be attached to this objection of Hering's, which is several times quoted in his works as his most powerful argument. Any one who reads this book to the end will be able to convince himself that astonishing disturbances of function can be tolerated by the heart and by patients, much greater disturbances than are required for the appearance of alternating action of the heart.

§ 43. *Pulsus Alternans in Literature*.—When we look through the literature on *pulsus alternans* in the light of the theory that we propounded in the last paragraph, the cause of the controversy that arose round this type of pulse becomes at once apparent, and we are able to come to a decision at least in some cases.

Since the ultimate causes of extra-systoles (*bigemini*) and *pulsus alternans* were unknown, it is not surprising that with their great external similarity to each other these two varieties were often confused, and that a controversy arose about them. But the positiveness with which some observers upheld *pulsus alternans* as a special type would lead one to infer that, besides the regular *pulsus bigeminus* that is produced by extra-systoles, there was really another form that could not be compared with it, and it is interesting to see how, up till quite recently, observers spoke for or against *pulsus alternans* according as they had once observed this rare variety or not. In judging of these cases of *alternans* we can now conclude with great probability that they are so when:—

<sup>1</sup> *I*de Appendix 5.

(1.) The phenomenon continues for weeks and months under various conditions, a rhythm that is not compatible with the occurrence of extra-systoles.

(2.) The alternans does not pass into other types of pulse, and is obscured at most for only a short time.

(3.) The difference in the length of the period before and after the small beat is always a very small one, whether this beat appears either a little earlier or a little later, or perhaps sometimes earlier and sometimes later.

(4.) The sounds of the small beats or non-extra-systoles on auscultation were only weak, but otherwise normal.

Keeping these four points in view, it is even yet not difficult to discover with great probability in literature cases of pulsus alternans, which certainly seems to be a very rare form. The absence of any time tracing, however, makes this posthumous diagnosis somewhat uncertain.

The original case of pulsus alternans, described by Traube,<sup>(112)</sup> was most undoubtedly due to an alternating action of the heart, in which probably the conduction-power as well as the contractility was affected. The delay of the small systole on the one hand and the continuation of the alternation on walking, sitting, or lying, on the other, confirm this hypothesis.

Fraentzel's cases exhibit different forms of pulse. On making a careful study of his communications on this question one is convinced that his cases, 1 and 3 (<sup>32</sup>, 1875), in contrast to the others, fulfilled the conditions of alternation of the heart completely. The following remarks may be quoted from the notes on his first case: 26th August, "Each moderately high pulse-wave is followed by a low one, and after it by a pause which is obviously longer than the pause between a high and a low beat. *This rhythm continues with perfect regularity.*" 28th August, "... One observes that to-day the rhythm is changed; the pause follows the big beat in such a way that the form of pulsus alternans which Traube described is now seen. In consequence of this the second small wave, that was previously observed, appears sometimes, *when it is seen in the pulse at all*, like a 'grace-note,' before the large one." 31st August, "The systoles of the heart and the pulse-beats were counted simultaneously, and it was found that the former were exactly twice as many as the latter, viz., 22 and 11 in  $\frac{1}{4}$  minute." On 5th September, the pulse was irregular. 14th September, exitus. Fraentzel further remarks

on this case: "The systole which had no corresponding pulse-beat was still perceptible by the fact that the systolic and diastolic sounds appear much weaker than in the systole corresponding to the preceding pulse-beat." In this case, therefore, we find the phenomenon continue first with a somewhat early-occurring small pulse-wave (it is remarkable that Fraentzel makes special mention of this fact), then with a delayed small beat (due to the additional disturbance of conduction); the small wave ultimately disappears, the heart-sounds (*i.e.* the systoles) become much weaker, and *the half-frequency with regular rhythm* appears, as every practitioner has observed again and again, towards the end of life.

Fraentzel's third case is very probably also one of alternation of the heart: "On 8th October, the very low pulse (120 per minute) was first observed to be regular, but had a peculiar rhythm. Every high wave is followed with perfect regularity by a low one, although the latter is not followed by such a long pause as is usually the case in *pulsus bigeminus*, and no variation can be observed in the intensity of the heart-sounds, which in themselves are very weak." "On 1st October the frequency of the pulse suddenly sank to 60 beats without any change in the medicine having been made. I immediately compared the heart-sounds with the pulse, and found that there was only one pulse-beat for every two systoles, but still no change could be detected in the intensity of the heart-sounds, although I examined the heart for a very long time for this." Subsequently the first form appeared again. *After the administration of digitalis* Fraentzel remarks: "To-day one observes a *pulsus alternans*, the first wave low, the second high, then the pause, and so on." This pulse also fully bears out the theory of an alternation of the heart's action.

The first of Sommerbrodt's cases (<sup>104</sup> 1877) can probably be put down as another one of alternation. It too showed a change, through a perfectly regular stage, from an alternation with an early-occurring small wave to one with the wave delayed. The short regularity on deep inspiration is specially characteristic; at the same time there is always a small variation in the rhythm which, as was explained above, can produce the alternation and also make it temporarily disappear (*cf.* my first case § 41). The alternation continued for four weeks without any *digitalis* having been given.

Schreiber <sup>(102)</sup> reports that in his first case he found the alternation for over a year without interruption. The cardiogram shows

that the systoles during this phase began with perfect regularity, a pure example of alternation of the heart. Still, Hering, who considers the cardiogram decisive on this point (it holds good in recording the action of the ventricle in experiment, but not in man, in whom the cardiogram shows something quite different, *cf.* § 25, p. 53), holds that this pulse shows the regular occurrence of extra-systoles, because on auscultation and palpation the small systole appears to come a little too soon. What was said in § 40, together with a glance at Fig. 21, will suffice to show that the condition found on auscultation is quite in accordance with the theory of alternation.

A beautiful example of *pulsus alternans* is found in the tracings taken by Huber (<sup>98</sup> 1891). Figs. 4 and 5 show it as it occurred during an attack of paroxysmal tachycardia. The transition from the regular frequent pulse into *pulsus alternans* can be followed with great precision, and all possibility of extra-systoles can be excluded.

The case which Dehio (<sup>99</sup>) described is not easy to classify. As far as his description goes the *allorhythmia* was not present regularly; the appearances both at the apex beat and in the pulse varied. It is impossible to come to a definite conclusion about the case, as there is no time marking in the short curves.

In Sansom's well-known book (<sup>101</sup> 1892) there is a case of undoubted *pulsus alternans*. So far as can be seen from the very instructive illustrations (Fig. 123), the small wave was slightly delayed. The *allorhythmia* continued from a first attack of Cheyne-Stokes' breathing up to the time of the patient's death, 109 days after. Sansom says of this case: "It is a perfect example of the alternating pulse, a more ample being always succeeded by a less ample tracing, each being perfect in all its elements. The irregularity is in volume only, and the cyclical sequence is invariable."

It is specially interesting that Mackenzie, who has made such a thorough study of the irregularities of the heart and pulse, and especially of "premature beats," has isolated two cases out of all the others he has observed.

Through the kindness of Mackenzie I am able to reproduce two tracings of undoubted *pulsus alternans* (Figs. XVIII. and XIX.). He says of the first tracing: "Here is a smaller beat  $s^1$  after every full beat  $s$ , and the tracing resembles an ordinary bigeminal pulse, with the exception that there is no prolonged pause after the

smaller beat  $s^1$ . Such pulses as these, however, are extremely rare, and I cannot tell what the significance may be. Another form of exceptional irregularity is when a smaller ventricular systole occurs, followed by a correspondingly shorter diastolic period (Fig. XIX.). This may be of the same nature as Fig. XVIII., but I give it separately, as the lesser beat shows as complete a wave as the larger beat. Occasionally, one finds a small beat recurring at the usual interval."

In this way, without giving any explanation, and so without any "bias" (*cf.* Hering, *loc. cit.*), this acute observer separates these forms of pulse, which we can now recognise as due to alternation



FIG. XVIII.



FIG. XIX. After Mackenzie.

of the heart, from the other cases of "premature beats," which he has described with such accuracy.

From this brief survey of the literature, which has no pretensions of being complete and takes no account of the cases of undoubted extra-systoles, it is seen that cases of real alternation, like those we have here described and traced to a disturbance of the contractility, had already been recorded, although it is only now that they can be interpreted with certainty. But, even now, it is only by carefully measuring the time in each individual case, by taking tracings of the apex beat and venous pulse whenever that is possible, and watching the case over a long period, that it will be possible to establish conclusively the presence of these forms of allorhythmia.

§ 44. **More Serious Disturbances of Contractility.**—From observations made on man we have seen that the weak systole in alternating action of the heart may become so small that it no longer produces a pulse-beat in the peripheral arteries. Whether

it may go so far in man that as the contractility is more impaired this small systole will disappear altogether cannot as yet be determined. In physiological experiments halving of the frequency is often seen (*cf.* § 40), and hence it is impossible to deny that it may also occur in the human heart. A still greater disturbance of contractility might perhaps lead to the dropping out of several systoles.

We must accept it as absolutely certain that disturbances of contractility can be manifested in arrhythmia in other ways, but then frequently in conjunction with disturbances of other functions. We shall refer to this more particularly in discussing the influence of the nerves on the heart (§ 59, &c.).

§ 45. **Causes of the Disturbance of Contractility.**—This is a subject about which little is yet known, and in addition to the many open questions which these discussions enable us to raise with regard to the finer details of the heart's action there comes a question of fundamental importance: *Under what circumstances is such a disturbance of contractility seen, not only in experiment but also in man, that disturbances of the regular rhythm of the heart appear?* Then comes another and no less important question: *What influences have the effect of increasing the contractility, a positive inotropic effect?*

As regards the first question, we know that, in the first place, great exhaustion of the heart impairs its contractility; a too high frequency, which, as we already saw, is able to diminish all the functions of the cardiac muscle, the conductivity most of all, can also reduce the contractility to a certain extent. The experiments of Engelmann, which have been already referred to, leave no doubt upon this point. That this may also possibly occur in man follows from the high frequency which was observed in many cases of alternation; the appearance of an alternating pulse during an attack of tachycardia (Huber's case) also points to this. We think we can regard the falling out of systoles in a case of great disturbance of conduction and of high frequency as an example of the myogenic self-regulation of the heart, modified to suit the condition; so in the same way we can perhaps look on the alternation as a suitable change in the succession of beats to help to restore the heart. When the contractility is very much impaired the small short systole weakens the heart less and gives it longer time to recover.

It cannot be doubted that asphyxia can produce a disturbance of contractility in the dying human heart, as it is able to do in the dying frog's and mammalian heart; the alternation, and particularly the regular rhythm of the heart with half-frequency, which are often observed towards the close of life, point to it as the cause.

Finally, all the various anatomical conditions that impede the work of the cardiac muscle, diminish the contractility. The destruction of numerous muscular fibres, as occurs in acute and chronic fibrous myocarditis, makes the work harder for the fibres that remain. Pericarditic adhesions and stretching of the cardiac muscle, from dilatation in valvular disease, or from over-filling of individual chambers (the auricles!) can exert an equally exhausting influence on the heart-muscle.

It has long been known that poisons can reduce the contractility, and this has been confirmed by the works of W. Straub, Magnus, Rümke, and others; it is, of course, still unknown what is the ultimate cause of these disturbances. Perhaps most light will be obtained on this matter through experiments made to determine the action of certain ions upon the contractility, like those of Loeb, Magnus, Göthlin, Langendorff and others.

There are substances belonging to the digitalis group, in particular antiar, that have a paralysing action on cardiac muscle. As Rümke observes, this fact compels us to be careful not to give large doses of digitalis, or continue its use long, in a case of pulsus alternans.

We shall consider the strong negative inotropic effect which stimulation of the vagus has on the heart more fully in the section on the nerve influences on the heart (§ 56, &c.).

It is still impossible to give a definite answer to the second question which was raised; it offers a very suitable and fruitful field for pharmacological research. It is very desirable that we should some day acquire some further knowledge about positive inotropic poisons or ions!

#### THE DISTURBANCES OF EXCITABILITY

§ 46. **The Idea of "Excitability."**—By the excitability of cardiac muscle one understands the susceptibility of the muscle to natural and artificial stimuli. In order to get a proper idea of this function, and to prevent any misunderstanding, it is absolutely

necessary to make it clear that excitability (or irritability) is a function which is measured not by the amount of reaction, as is so often done, but by the strength of the smallest stimulus that is just sufficient to produce a contraction. Far too much has been spoken about increased or diminished excitability in stronger or weaker action of the heart. The capacity of the cardiac muscle for work (*Leistungsfähigkeit*), which is seen firstly in the contraction, and secondly in the conduction of stimuli, is something quite different, and connected with different molecules, from the capacity of responding to stimuli (*Anspruchsfähigkeit*). As the contractility is measured by the size of the contraction, and the conductivity by the speed with which the contraction travels through the muscles, the minimal effective stimulus must be determined in order to judge of the degree of excitability; it is low when the excitability is high, and *vice versa*. Those influences that alter the excitability are called, after Engelmann, positive and negative bathmotropic, as was already explained in the first chapter. We must also imagine that there is a definite substance capable of excitation or a definite grouping of molecules or ions, and as they vary in number the excitability rises and falls. Engelmann compares the stimulation of the muscle with the firing of a gun (<sup>28</sup> pp. 22, 23): "Just as the powder on the powder-pan that is set off by a stroke or spark, or the pin that is driven into the percussion-cap of the cartridge by pressure of the cock does not itself supply the force of the shot, but only does it indirectly by setting free the chemical energy lying dormant within the barrel, so the irritable substance in the muscle that is stirred up by the external stimulus does not of itself supply the actual energy that becomes manifest in the contraction and the formation of heat, but only indirectly gives rise to the process of real excitation, the contraction by setting free the chemical energy that is accumulated in special molecules at special places in the interior of the muscle cells."

If in any way we conceive the excitability of the heart-muscle purely as its susceptibility to stimuli, as we are bound to do in the present position of the physiology of the heart, we shall find very few physiological facts, all of very recent date, that can give us any clue to the discovery of bathmotropic disturbances in man. This section will therefore give us very little of a positive character. Still that is the very reason why it is so urgent that we should at least take up the problem of the disturbances of excitability in

human pathology. It is only when we have clearly in our minds the object of our research, as well as the method and means by which it is to be investigated, that it will be possible to ultimately obtain a satisfactory answer to this problem. The following remarks are offered only as an attempt in this direction.

§ 47. **The Excitability of the Cardiac Muscle in Experiment.**—In experiments the excitability of any organ is estimated by the minimal stimulus that is sufficient to excite it. Experiments of this nature have been carried out by Engelmann<sup>(19 28)</sup> for the cardiac muscle in a most exhaustive manner. I must again refer to the frequently quoted work of W. Straub,<sup>(100)</sup> in which the excitability was also correctly determined. The papers of Öhrwall<sup>(85)</sup> and Göthlin<sup>(87)</sup> are also worthy of mention.

We know that every systole puts the heart into a refractory phase. During the systole, and for a very short time after it, the heart cannot be excited, not even by the strongest stimuli. After the systole the excitability grows again along with the contractility, conductivity, and the autochthonous stimulus-matter itself. But we are also aware that the four functions of the heart do not normally increase exactly in the same measure, and from various causes, such as asphyxia, poisoning, and nerve influences, may undergo changes within wide limits independently of each other.

If we suppose the excitability uniformly increased, we must then assume that the "irritable material" (the "powder in the pan") is built up again more quickly than normally after the systole. Hence the moment of excitation is sooner reached than normally by the stimulus-matter, which is also increasing after the preceding systole, the cardiac cycle becomes shorter, and the frequency is increased.

If, on the other hand, we imagine the excitability to be uniformly diminished, we must then assume that the "irritable material" is reformed less rapidly. The motor-stimulus, which has been increasing during the usual interval up to the point of its formerly effective strength, now finds the muscular fibres still in an insufficient state of excitability; the stimulus, like the "irritable material," must go on increasing until they bear such a relation to each other that the stimulus can have effect. Diminished excitability therefore lengthens the cardiac cycle, and reduces the frequency. The reduction of the frequency can be demon-

strated in almost any dying heart, and is also brought about by all kinds of influences. Beautiful examples of the slow reduction of the frequency are given, for example, by Öhrwall (<sup>85</sup> Fig. 24), Straub (<sup>107</sup> Fig. 4), and in most tracings of dying hearts which are found in literature.

We must, however, at once point out that the increase and decrease of the automatic stimulus-production produce the same symptoms, as will be more fully discussed in the next section, and so a quick or slow action of the heart may be due to a rise or decline of either of these functions, or of both together.

Another consequence of a general increase in the excitability of the heart is, that any extraneous, abnormal stimuli can excite the heart to contraction more readily than when the excitability is lower, and hence there is more opportunity for the occurrence of extra-systoles.

As yet we have assumed that the excitability is uniformly increased or diminished throughout. When it is uniformly diminished systoles will not fall out, for the following reasons: We know that the production of the motor stimulus goes on continually until the stimulus matter is destroyed by a systole; but when the excitability is uniformly diminished, and therefore also in the muscular fibres in which the automatic stimuli are generated, the stimulus matter will not take effect till later, it will set up a delayed contraction, and so will not be destroyed till later. But it is different when the excitability is diminished only at certain points and not uniformly. If the excitability in the muscle cells at the ostia venosa remains of average intensity, but is reduced farther down in the cardiac muscle, the stimulus will produce a contraction at the ordinary time. As long as the excitability of the rest of the cardiac muscle is still sufficient, a systole will be produced of normal size, and after the usual period of rest; but, as soon as the excitability has become too much reduced, the contraction which began at the venous ostia will travel as far as the refractory spot and stop there. The next stimulus, however, will not find the muscle refractory, and so will produce a contraction. Thus a beat is missed when the excitability is too low. In this way systoles may fall out periodically until finally the half-frequency is reached.

When only the excitability is affected, the conductivity and contractility still remaining good, the periodic falling out of systoles

will necessarily take on a strictly rhythmical character, for we do not find here the lengthening of the interval  $V_{e_s} - V_s$  or  $A_s - V_s$ , which is caused by an arrest of conduction, and produces a regular variation of the ventricular periods, as was discussed before; nor do we meet with an alternating stage, due to a diminution of the contractility, as a step towards the half-frequency. If disturbances of these functions are present, we can then at most suppose that there is also a disturbance of excitability.

It has been most conclusively shown by W. Straub in his experiments with antiar that the disturbances can occur simultaneously; but that there are also strictly regular periods is shown by the work of Öhrwall and others.

A remarkable condition in a disturbance of contractility is reported in a paper by Von Kries.<sup>(65)</sup> He reduced the excitability of the heart by the application of cold at a certain point, and then observed that systoles soon began to fall out periodically until there was a condition of half-frequency. If now the cooling was continued longer, this half-frequency was halved again, and then another time; he always observed  $\frac{1}{2}$ ,  $\frac{1}{4}$ ,  $\frac{1}{8}$  frequency, but never  $\frac{3}{4}$ ,  $\frac{5}{8}$ , or  $\frac{7}{8}$ . The explanation which he gave for this phenomenon is perfectly obvious: "Suppose it is the warmest part from which motor stimuli proceed (as in our experiments) at the rate of  $n$  per minute. As we pass from this point in the direction of the normal stimulus-conduction we first come to the adjoining parts, the temperature of which is a little, but not very much, lower, and permits of  $\frac{n}{2}$  contractions in the minute. As we go farther on, we naturally come to parts which, from their temperature, would be able to make  $\frac{n}{3}$  contractions per minute. We must, however, bear in mind that they are not directly connected with the parts that sent out  $n$  stimuli, but only indirectly through fibres which are capable of  $\frac{n}{2}$  systoles. If this frequency exceeds their capacity for work, they can only respond to half of it, i.e. to  $\frac{n}{4}$  systoles." When now in any particular experiment we know that the excitability is always longest preserved in the neighbourhood of the venæ cavæ, and that the uniform diminution always proceeds from the apex of the heart, or at least from the ventricle, it is quite possible that other conditions besides the application of cold may reduce the

excitability always by half. We have already spoken of this peculiarity in dealing with heart-block (§ 36).

§ 48. **Diminution of Cardiac Excitability in Man.**—When we now come to consider whether there are any forms of allorhythmia in man that must be regarded as due to an abnormal increase or decrease of excitability, we find that this is a subject about which really nothing is known. All that can be said about it at present is, that—

A diminution of excitability at the venous ostia will cause a reduction in the frequency of the heart. I have, however, as yet been unable to find any signs to help us in determining whether there has been a reduction of the stimulus-production instead of the excitability, or a reduction of both; still, I have no doubt that future physiological discoveries will enable us to do so.

A serious disturbance of excitability below the venous ostia can lead to the periodic missing of beats, to half-frequency, and finally to quarter-frequency, and so on. It is often impossible to say definitely whether the diminution of excitability is or is not the cause of the dropping of beats in any given case. Still, there are certain signs in this instance, as was already pointed out. We can assume the diminution of excitability to be the *sole cause* only in cases where the rhythm of the heart *remains perfectly normal*. If the allorhythmia, due to a disturbance of conductivity, appears at the same time, or is observed as a transitional form, we must first put down the disturbance of this function as the cause of the periodic dropping out of beats or the half-frequency, as is seen in the case which was discussed in § 33, and illustrated by Fig. 4 *a*, 4 *b*, and Fig. 16. When we find a transitional stage of alternating action of the heart, we must first think of a disturbance of contractility. If we observe a frequency of  $\frac{n}{2}$  and  $\frac{n}{4}$

exclusively, but never one of  $\frac{n}{3}$  we should perhaps infer that the excitability is impaired, although a disturbance of conduction might lead one to suspect the same condition.

I should like to state explicitly that these remarks have been put forward merely as a guide to the analysis of the forms of irregularity with which we are at present dealing. As progress is made in the investigation of the heart from the physiological side, a great portion of the ideas here expressed will perhaps prove wrong, but I shall gladly accept such a result as a gain.

§ 49. **Increase of Cardiac Excitability in Man.**—When there is an increase of the cardiac excitability in man, various disturbances of the rhythm may be expected. We are actually compelled to assume that increased excitability, or hyperæsthesia of the heart, plays an important part in pathology. The increased susceptibility to normal and abnormal stimuli is an important factor in the production of many disturbances in the functions of organs; and an increase in excitability is very frequently a symptom, and perhaps also the cause of, or at least concomitant with, considerable diminution in the most important functions of an organ. Irritable weakness, a condition in which the organ responds readily, but after a short time refuses to work satisfactorily, is too often met with in the heart. It is remarkable that in many cases, both experimental and clinical, the excitability is increased towards the end of life (*cf.* Öhrwall and others).

An increase of excitability will, *ceteris paribus*, in the first place shorten the cardiac cycle, and in the second expose the heart to the action of all kinds of stimuli, which otherwise have little or no effect. Hence, in conditions where from other symptoms we can assume there is hyperæsthesia of the cardiac muscle, we find a strong reflex effect on the heart, an increase and diminution of the rate of the heart's action with any mental excitement, with affections of other organs, and so on. In these cases, however, there is a great tendency to extra-systoles (*cf.* § 26). That they are often the result of hyperæsthesia of the heart is shown by the fact that, with general tonic treatment, the irritable weakness of the heart, as well as of other organs, and with it the occurrence of extra-systoles, may diminish or disappear altogether.

§ 50. **Causes of Disturbances of Excitability.**—It is difficult to determine what are the causes of disturbances of excitability in man. We must appeal on the one hand to clinical experience, which has failed as yet to give any precise data, and on the other to the results of physiological experiments in which the determination of the excitability under various influences has only been commenced.

These two sources of our knowledge lead us to the definite conclusion that fatigue or over-exertion may be a primary factor in the reduction of excitability, as well as in "irritable weakness." W. Straub has shown that certain poisons, *e.g.* from the digitalis

group, can reduce this function; but it is very considerably influenced through the nervous system. Engelmann<sup>(28)</sup> has recently brought forward conclusive proof of a bathmotropic nerve influence. It can hardly be denied or doubted by any physician of experience that in a "nervous" person this influence may predominate. This short account shows the urgent necessity of earnest experimental work being done to enable us to give a satisfactory answer to the following questions: What influences that are found in man can change the normal excitability of the cardiac muscle? What influences, and, more particularly, what drugs, can diminish the excitability when it is increased, and raise it when it is too low? For it is only when these problems are solved that the study of the disturbances of the cardiac rhythm, due to abnormal excitability, can yield any practical result.

#### THE DISTURBANCES OF THE AUTOMATIC STIMULUS-PRODUCTION

§ 51. **The Production of the Motor-Stimulus.**—The disturbances of the cardiac rhythm that arise from changes in the production of the motor-stimulus, and in a measure those that are the result of changes in the excitability, offer a certain contrast to all the other forms of allorhythmia that have been described. When extra-systoles occur, the original rhythm of the heart is not disturbed, or, if the extra stimulus can come to the ostia venosa, it is only disturbed in a definite manner. Considerable disturbances in the conduction, contractility, or excitability (in the last-named, when the disturbance is below the ostia venosa) lead to a characteristic change of the undisturbed original rhythm into one of the forms of allorhythmia above described, the periodic missing of beats, alternation of the height of the systoles, &c. The stimulus-production, however, *ceteris paribus*, controls the original rhythm of the heart; the irregular production of stimuli leads to *true arrhythmia*.

We must at the same time remember that the moment of stimulus is determined not only by the strength of the stimulus but also by the degree of excitability then present in the muscular fibres. When there are variations in the rhythm, therefore, we shall always be in doubt whether we have to deal with changes in the stimulus-production, or in the excitability, or perhaps in both. In experiments this point can be decided by determining the lowest stimulus necessary to excite a contraction, but clinically it is usually

impossible to do so. When the muscle cells are not in a uniform state at the seat of stimulus-production, as we are bound to assume in pathological conditions, but show local differences in function through degenerative or other processes, the matter becomes so complicated that we must for the present waive all claim to an accurate knowledge of the causes of arhythmia.

If in spite of that we now proceed to discuss the changes in the stimulus-production, it is only done for the purpose of indicating the main difference between these changes and those of other functions, and maintaining that it is very necessary to take this function into account in the analysis of irregular action. In this way it may be possible to find out on what lines this complicated problem should be further investigated.

Before we begin to discuss the disturbances of stimulus-production, it should be once more emphasised that we must assume the strength of the stimulus immediately after the systole = 0, and the excitability is abolished; during the diastole new stimulus matter goes on being formed, and the excitability gradually returns, until the relation between these two factors comes to the point that the stimulus has effect and produces a contraction. So long as a contraction does not take place, the stimulus-matter increases until a contraction is produced and destroys it. Whenever therefore we observe the falling out of systoles while the original rhythm is preserved (halving, and so on), we must assume that a minimal contraction, perhaps one confined to the cells which generate the stimulus, has at all events occurred. But we have still no means of measuring the strength of the stimulus provided it does not produce any contraction; no electrical phenomena, so far as I am aware, are known to accompany the production of stimuli. Leaving out of account the primary and secondary changes of excitability at present, we must determine what are the results of *increased*, of *diminished*, and of *irregular stimulus-production*, and bear in mind that the cause of these changes cannot only be in the heart-muscle itself, but also comes from outside through the nerves.

§ 52. **Increased Stimulus-Production.**—The result of an increase in the production of the motor-stimulus, as we have described it, is that it reaches the necessary strength again after a systole in a shorter time than normally, the cardiac cycle is shortened, the frequency increased. We cannot, however, yet say that every increase of frequency is due to increased stimulus-production; we

must remember that increased excitability can have the same effect. It is also quite obvious that a diminution of excitability may counteract or indeed override it.

We have already seen (§ 3) that automatic stimulus-production is a property that belongs not only to the muscle cells situated at the ostia venosa, but also to the cells in the other parts of the heart to a less degree. Hence portions of the heart-wall that are clamped off or excised have also the power of making rhythmical contractions under suitable conditions. And the cases of Chauveau and Mackenzie, discussed in § 35, show in a very striking manner that the same property may be possessed by the human heart. In those cases the conduction from auricle to ventricle had become so far impaired that the ventricle was left to contract regularly in its own rhythm, independently of that of the veins and auricle, and so keep up the circulation.

In § 26 we have already referred to the question which Engelmann raised, whether the auricle and ventricle can perform independent contractions when their power of automatic action is increased. Such independent contractions could then interpolate themselves between the systoles which proceed from the veins, and behave exactly like extra-systoles, producing a compensatory pause. This is certainly a possibility that must be taken into account; those forms of arrhythmia which represent the highest type of irregularity, *delirium cordis*, give one the impression that a great number of the systoles recorded in a tracing are only partial systoles, contractions of only portions of the heart-wall. Still, in most cases it is scarcely possible to determine whether these contractions are set up by autochthonous or by extraneous stimuli (*cf.* § 77-§ 83).

§ 53. **Diminished Stimulus-Production.**—A diminution of the stimulus-production reduces the frequency of the pulse, just as increased stimulus-production raises it. Yet we must bear in mind in this case also that a bathmotropic effect, an increase of the excitability, can obscure the negative chronotropic effect. The study of purely chronotropic changes in man is met with considerable difficulties, and hence it is usually almost impossible to decide in any individual case whether negative chronotropic or negative bathmotropic influences are at work to cause the slowing of the pulse. But in experiments one obtains an opportunity of testing the excitability, conduction, and contractility by artificial stimulation while the stimulus-production is reduced. In this way Engel-

mann was able to abolish the stimulus-production alone, without a disturbance of any other function. He has lately recorded an example of such an experiment (<sup>25</sup> p. 4): while the heart was at a standstill he was able to produce perfectly normal contractions by applying weak electrical stimuli to the veins.

Very complex relations between stimulus-production and excitability arise in hearts that are very seriously affected, as the works of Oehrwall and others show. We cannot go into these relations further here, especially as it has not yet been possible to make a control observation in man, while the results of even experimental work have not yet been fully established.

§ 54. **Irregularity of Stimulus-Production.**—When the production of the motor stimulus is irregular, the rhythm of the heart becomes the same; it is then a *real primary arhythmia*.

This type of arhythmia is found in man as well as in experiment. As regards the causes of such changes of rhythm, not only can all possible influences that have any effect on the cardiac muscle, and particularly on the muscle cells at the mouths of the great veins, manifest themselves in this way, but chronotropic influences take a free part in controlling the heart by reflex action through the nerves. These chronotropic influences shall be taken up more fully in the next section. But it should be observed here that the action of the heart in man is probably never absolutely regular. Even in a person with perfect health and at rest there are variations in its frequency; indeed, there may be very considerable differences in the length of the periods, and yet the heart is capable of doing its work. Of course there are persons with an extremely regular pulse; there are others in whom it is almost invariably irregular. Speaking generally, one may say that irregularities are very frequently met with in neurasthenic persons; and we shall see that some authors go so far as to speak of a special neurasthenic arhythmia.

If we observe for a considerable time the heart of a person that shows more than the normal variations in the periods, it is almost invariably found that the variations themselves appear periodically. The arhythmia that goes up and down with respiration is an example of this kind (*cf.* § 58).

If one looks for an absolutely non-periodic, irregular arhythmia in any long series of pulse tracings, they are found much less frequently than one might at first expect. It is easy to give examples, but, as far as my experience goes, they are much fewer

than the forms of arrhythmia in which a definite, constantly recurring type is found.

As examples of this, I would refer the reader to Fig. 24, Plate V., taken from a woman 82 years of age, and Fig. 25, Plate V., taken from a man of 76. These tracings show very plainly a more or less regular alternation of groups of long and short periods. In Fig. 26, Plate V., we see an example of a really irregular arrhythmia, caused by a true disturbance of stimulus-production; with the aid of the cardiogram which is also given, we can exclude other disturbances of the rhythm from extra-systoles, &c.

If the irregularity is more marked, it may easily be impossible to exclude the presence of extra-systoles with certainty; an example of this is seen in Fig. 5, Plate II. In this case there is undoubtedly very marked irregularity of stimulus-production at the ostia venosa, but it is not clear whether it is entirely a pure primary arrhythmia, as was already pointed out in §§ 18, 25. In analysing these forms, however, one should take note of what is said in §§ 77-83.

Irregular stimulus-production is very often accompanied by other irregularities, as one would expect. We shall refer to this fact again and again in considering the action of the nerves on the heart and the clinical types.

This meagre account of the primary disturbances of stimulus-production is naturally not sufficient to give one a deep insight into primary arrhythmia in man. It will be necessary to carry out experiments in this direction before further progress can be made, and the causes of irregularities, apart from those due to nerve influences, can be traced. Still it was of fundamental importance to establish the fact that there is a true primary arrhythmia in man, which differs entirely in its cause and practical significance from that which is the result of disturbances of other functions or of extra-systoles. In the case of the latter it is a regular rhythm, which becomes irregular through disturbing influences (*Pararhythmia*, cf. § 23); in the former it is an essentially irregular action of the heart, a *true arrhythmia*.

#### THE INFLUENCE OF THE NERVES ON THE HEART

§ 55. **The Influence of the Nerves on the Heart.**—Since the study of the physiology and pathology of the heart was commenced we have known that the central nervous system, as well as the

stimulation of certain nerve fibres, is capable of exerting a strong influence on the rhythm and force of the heart. Since its very movement was supposed to be derived from the nervous system it was natural to refer all its irregularities to an inhibition or excitation of nerve elements. Increase and decrease in the rate of the heart were the results of stimulation of the sympathetic and vagus, and hence it was thought that irregularities must be explained by a combination of these two factors. Now, however, our views on the origin of the cardiac movements are quite changed; the conditions on which the automatic action of the heart depends are to be found in the four functions of the cardiac muscle fibres, and stimulation of a nerve produces an effect from the fact that it produces changes in these different functions.

It now falls to us to analyse the action of the nerves upon the individual properties of the heart-muscle, not merely in experiment, but also at the bedside; and it is all the more important in the latter case because nerve influence almost invariably makes itself manifest by changes in the rhythm, by arhythmia. Physicians have long been driven to the diagnosis of *cardiac neuroses* in cases of well-marked arhythmia in perfectly healthy hearts. But in order to determine accurately and correctly whether some nerve influence is really at work or the irregularities are due to changes in the functions of the muscles themselves, it is absolutely necessary to investigate the forms in which nerve influence can manifest itself. Such an investigation in human pathology, however, has scarcely ever been taken up systematically. We should expect an endless number of different forms in this field, when we consider the infinite number of combinations which can arise from the effects of nerve influence upon the different properties of the heart. In experiment this extraordinary difference in the influence of the nerves has long been recognised; and it is most likely that an equally great variation in the form of the rhythm will be found in man. In analysing these forms we shall have to fall back upon the results of experiments that have been carefully analysed and interpreted; and in this respect the works of Engelmann, to which reference has so often been made, will be thought of first, for the nerve influences are here found analysed down to the minutest details, with the aid of carefully and critically selected methods. When Engelmann takes up the analysis of the nerve influence in man, I must refer the reader to his original papers; it would be impossible to give any adequate

idea of their valuable contents here. All who are interested in this matter must read the papers themselves; a perusal of them will fully repay them, and they will also find there a full account of the literature (*cf.* Engelmann <sup>24, 29</sup>). We can make no claim to giving a comparatively full and detailed survey of the literature here; we have kept it in view only so far as it directly bears upon the examples of pulse changes through nerve influence and the explanation of them which are given here.

In the introductory part of this book (§ 8) and in the discussion on the disturbances of the various functions, it was stated that the "slowing" and "quickening" of the heart's action that may result from nerve influences must now be regarded as quantitative positive and negative changes of the various functions of cardiac muscle. It is necessary to distinguish between those influences, because the functions can be separately affected. In the first place there are positive and negative *chronotropic* influences which regulate the length of the cardiac cycle, because they respectively increase and diminish the automatic stimulus-production. Secondly, *bathmotropic* influences increase or diminish the excitability of the muscle. Then there are *dromotropic* influences; they control the conduction of stimuli, and hence the progress of the conduction through the muscle. Lastly, *inotropic* influences control the contractility, and are called positive and negative according as they increase or diminish the contractility.

It is hardly necessary to do more than mention that an almost endless variation of symptoms may result from the simultaneous action of these influences. The number of combinations, and with them the difficulty in analysing these irregularities, is further increased by the secondary influences of the systole, which are blended with those through the nerves; thus increased frequency of contraction will exert a negative influence on the other functions, while diminished frequency gives them more time to recover. The changes of excitability influence the number of beats, an arrest of conduction may lead to the falling out of beats, and negative inotropic influences may have a favourable effect on the other functions in many cases.

With this blending of the various influences it is exceedingly difficult, even in experiment, to pick out what is of essential importance. It is therefore quite obvious that in a living person it is extremely difficult, nay, frequently impossible, to obtain an accurate

knowledge of what is taking place in the heart; and it is only with extreme caution that one can attempt to analyse these irregularities in man. There is, moreover, the additional difficulty that the arterial pulse gives merely an indication of the action of the left ventricle. In the previous sections we saw often enough that the action of the ventricle may be quite different from the original rhythm at the ostia venosa. On that account too the greatest caution is required. But since Mackenzie showed in his valuable book on the pulse how important are the inferences that can be drawn from the venous and the liver pulse, besides the tracings obtained at the apex beat and the radial, and how it was actually possible in favourable cases to register the action of the four chambers of the heart simultaneously, great progress in the analysis of nervous arhythmia can be expected in the future: all that is given here can only be called an attempt in this direction, although it certainly contains some remarkable cases.

§ 56. **General Characteristics of Nerve Influences.**—It is often very difficult to determine, in any given case of arhythmia, whether it is caused through nerve influence, or is the result of changes in the muscular fibres. No general rules have yet been made to help one to distinguish between the two forms. The term “neurosis” was too much used, when it was impossible to find any anatomical basis for any disturbance of the heart’s action. If we inquire into the matter more carefully, some general characteristics can be recognised.

When the cardiac muscle itself is affected, when *e.g.* the contractility is impaired, the conduction is deficient, the stimulus-production or excitability is altered, when, in other words, “myogenic” disturbances are present, we may expect that the resulting disturbances of rhythm will have a more constant uniform character, and continue uninterruptedly for a considerable time. Thus in cases of regular intermission from a disturbance of the conduction, or in those of real pulsus alternans, these abnormalities continue for weeks and months without a break; we could not expect anything else. The muscular fibres of a heart that have lost their conductivity or contractility to a large extent cannot recover this function again immediately, unless it is slightly increased for a short time by other influences through the nerves; this increase, however, can only last a short time, and will soon be followed by a more marked disturbance of rhythm from exhaustion. The cases of regular intermission and alternation that were reported bear this out, and we came to

the conclusion that in those cases these disturbances were located in the muscle cell, *i.e.* were "myogenic" in character.

If, however, we try to conceive what symptoms will arise from the effect of nerve influence on the heart, it will be at once obvious that they are bound to be very variable for several reasons. We must assume that in a live person the heart is always under the influence of the nerves, or at least falls into a state in which their influence can at once have effect; the first effect of their influence then will be to make the cardiac functions vary above or below a medium standard. But we know furthermore that, generally speaking, the nerve influences have a more capricious character, and the changes they produce on the functions are more paroxysmal in nature. The "paroxysms" can last for a longer or shorter time, and may be more or less fully developed. We know from experimental work (*cf.* Engelmann, *loc. cit.*) that the same reflex influence on the heart, especially when it is acting at different places with different intensity, can produce the most varied effects, positive and negative, on the individual and combined functions. All these facts warrant us in expecting that nerve stimuli will affect the heart in a paroxysmal and extremely varying manner. When now we find in "myogenic" disturbances exactly the opposite condition, *viz.*, a more uniform continuance of the disturbance, we possess in this fact a very important sign to enable us to distinguish between these two forms of arhythmia.

There are other signs pointing to nerve influences, *e.g.* any other symptoms of nervous affections, such as general neurasthenia, or more serious pathological conditions, symptoms of cerebral or spinal disease, epilepsy, or apoplexy, &c. There is no lack of examples of this kind, as we shall see.

§ 57. **The Effects of Chronotropic Nerve Influences.**—In treating of the changes in the cardiac functions from the influence of the nervous system, the *chronotropic* changes deserve special attention. They are without doubt the most important and most necessary, and hence also the most frequently observed changes in the heart. Even in healthy persons we continually meet with changes in the frequency of the pulse, which we can at once admit to be the effect of the adaptation of the heart to external circumstances. They are of great importance clinically, and from the careful researches of F. B. Hoffmann<sup>(55)</sup> on the functions and anatomical distribution of the nerves in the heart, we know that there are special nerve

fibres which enter the sinus of the frog's heart and end there, *i.e.* at the spot where the automatic stimuli are generated; these will necessarily have a considerable chronotropic influence. The results of Hoffmann's work, which we cannot go into fully here, tend also to show that in all probability there are special nerves that can be dissected out for influencing the other functions (*cf.* <sup>66</sup>).

Pure chronotropic influences manifest themselves by changes, *viz.*, an increase or diminution of, in the frequency of contraction. Such influences are not unknown in health as well as in disease; expectation, suspense, attention, fright, terror, make the heart beat more slowly or rapidly. These psychical effects can only affect the heart through the nerves. It often looks as if the influence is really a pure chronotropic one, especially in cases where the frequency is low; and yet the force and progress of the contractions remain the same. But if the height of the systoles still remained the same with a high frequency, when each systole is followed by a very short pause, it could only be explained by supposing a positive inotropic influence was also at work.

The influence which the mind has on the rate of the heart has been very thoroughly investigated by Winkler.<sup>(125)</sup> He established the fact that in any mental operation the pulse becomes more rapid from the very moment when the attention is concentrated on the task that is set (*e.g.* working out a simple sum in arithmetic), and becomes slow again when the mental work is done.

Generally speaking, *great variations* in the frequency must be attributed to some new influence. It will also be possible to ascribe a constantly frequent pulse, found in many pathological conditions, to a direct action on the cardiac muscle, if it can be assumed that there is a constant rise of nervous activity under the same conditions, as, for example, in fever.

A special and extreme form of increased frequency is found in paroxysmal tachycardia. This disease shall be discussed more fully in the clinical part of this book; but we must point out here that these paroxysms may be due to a very strong positive chronotropic nerve-influence, apart from the question whether we must assume a paralysis of inhibitory nerves or a stimulation of accelerating nerves in such a case.

Positive chronotropic influences are usually combined with those affecting the other cardiac functions. Numerous instances of this kind are met with in practice; for example, the case where

the contractions are not only more frequent but also stronger through a positive inotropic influence, a condition recognised subjectively and objectively as "palpitation." And in experiments chronotropic influences are almost invariably accompanied by others: examples of these may be found in the more recent works on vagus stimulation by Engelmann, Muskens, and others. Examples of cases fully analysed are also given by Engelmann (<sup>19</sup> p. 50, 52; <sup>24</sup> almost all the figures, &c.).

The negative chronotropic influence of the vagus has been the subject of special study. Inhibition of the heart, similar to what can be produced experimentally by weak stimulation of the vagus, occurs in man and has long been recognised. In these cases all that can frequently be seen is a prolongation of the cardiac cycle. An example of this is given in Fig. 27 *a* and *b*, Plate V. In the right half of Fig. 27 *a* the period length, which in other parts of the tracing usually amounts to 18–19 ( $\frac{1}{2}$  secs.), is increased for some time up to 21.5. In the left half of this figure, and more particularly in Fig. 27 *b*, the systole is so much delayed in places that one might well think they were intermissions caused by extra-systoles; but there was neither any sign of a premature wave in the pulse tracing, nor any sound of an extra-systole to be heard on auscultation; nor was an extra-systole ever once observed throughout a long period of observation of this patient, a neurasthenic woman forty-two years of age. Moreover, all subjective symptoms of extra-systoles were wanting, and yet it was remarkable that the patient felt exceedingly unwell and giddy, while the pulse was slow. On comparing the tracings given here with those of Engelmann above mentioned, one is at once struck with the perfect similarity between them. A similar pulse tracing is given by Hoffmann (<sup>54</sup> p. 188), and others; while examples of a slight retardation of the pulse are probably known to every physician. I would further observe that many of the cases of what Mackenzie calls the "youthful type of irregularity" are probably due to this disturbance. The cases which Hering (<sup>48</sup> p. 14) describes and designates by the name of *pulsus deficiens* might also perhaps be included in this group. It is at once apparent that these cases show the presence of a nerve influence from the variation of the phenomena. And yet Fig. 27 *a* shows that it need not be exclusively a chronotropic influence that is causing this arrhythmia: in this figure a negative inotropic influence is also at work at the moment when the

longest period occurs, this influence showing itself at \* by the reduction in the height of the wave (which cannot be attributed to a shortened period). Moreover, the blood-pressure makes a sudden and slight fall at this beat, as is seen from the fall in the pulse tracing.

Even a very small nerve influence like this is very complicated. And in analysing similar cases one must always bear in mind that extra-systoles, arising in the neighbourhood of the ostia venosa, can really lead to a missing out of ventricular beats. Hering (<sup>43</sup> p. 16) describes cases of this kind, but gives no diagrams. Engelmann had already pointed out this phenomenon, and explained it most conclusively on the principle of the "myogenic self-regulation" of the heart which he analysed (*cf.* § 11, p. 24). It must also be remembered that changes of excitability through nerve influence may lead to an increase in the period length. It will often be scarcely possible to say definitely what function is affected in such cases.

A case of extreme negative chronotropic influence may be given here. But in this case, too, it is impossible to say whether other influences, such as bathmotropic, are not also at work, although the changes affect only the period length. The patient is a man 27 years of age, well built, and shows no sign of organic disease of the heart. Since he was 15 years old he has suffered from time to time from attacks of irregular palpitation. He says his heart then stands still, he becomes giddy and sometimes even unconscious, but has never exhibited any symptoms of epilepsy. He cannot give any cause for these attacks; he has never suffered from any serious infectious disease like influenza, or from rheumatic fever. When he was examined his pulse was very frequent and irregular, but sometimes suddenly became extremely slow and still irregular. I was fortunate enough in being able to take a tracing of one of these sudden changes; it is reproduced in Fig. 28, Plate VI. The upper tracing is the cardiogram, the lower is a tracing from the radial, and the time-curve is in  $\frac{1}{10}$  seconds. The irregular frequent movement stops quite suddenly, and is replaced by a very slow one. The heart remains in absolute rest during the long pause, as the cardiogram shows. We are bound, in my opinion, to assume there is here a negative chronotropic influence, an inhibition of the stimulus-production, for there are no signs of a disturbance of conduction or a diminution of contractility. If there were, or, in other words, if systoles dropped out, one would rather expect the rhythm to be prolonged in a definite manner, *e.g.* a half-frequency,

as is observed, say, in heart-block. During the whole length of the attack of bradycardia, which I was able to observe and record for a considerable time, I could not find a trace of regularity. The longest period I observed measured 56.5 ( $\frac{1}{2\frac{1}{2}}$  secs.), i.e. it lasted 2.3 seconds! It is no wonder that the man became giddy from cerebral anæmia during these pauses, and even unconscious perhaps from the continued slow action of the heart.

There can be no doubt that this was a case of nerve influence. How such a strong influence can be discharged from the central nervous system I cannot as yet say with certainty. Only in this connection I must not omit a reference to Friedenthal's work <sup>(24)</sup> on sudden death from stoppage of the heart; in which an attempt is made to explain the fatal influence on the heart as proceeding from the medulla oblongata. In this chapter we shall have to treat of many other cases of negative influences probably arising in the central nervous system. As regards this case that I have quoted, I should like to add that after psychical treatment, supplemented by bromides and iodides and rest, the patient was much relieved from these attacks. When he came to see me again some months after, his pulse was perfectly regular, but soft, small, and very frequent (120 per minute).

§ 58. **Periodic Chronotropic Variations.**—Regular periodic variation in the frequency of the heart is a phenomenon with which we have long been acquainted. The most familiar example of it is that which occurs synchronously with, and undoubtedly depends on, the respiration. It is not a question here of the influence on the height of the pulse-wave which may possibly lead to "pulsus paradoxus," but of an increase in the rate of the heart during inspiration, and decrease during expiration. Lommel <sup>(27)</sup> has recently made a very careful and thorough research into this phenomenon; he has given a fairly full *résumé* of the literature on this subject, so that I need only refer to his valuable work here with regard to the proof that a nerve influence is at work in this variation. Lommel comes to the conclusion that this phenomenon is, clinically as well as experimentally, purely of nervous origin, for it is not a typical symptom of any organic disease of the heart, but it is one of neurasthenia; at the same time we do not mean that it cannot occur in cardiac disease. Lommel puts forward very strong proofs for his theory. The variation in rhythm does not depend on a variation in blood-pressure, it stops immediately during apnoea,

and is not dependent on diseases of the heart. We are bound to assume, as Lommel does, that the cause of this variation lies in "an excessive susceptibility in the inhibitory centre of the vagus." This view is finding considerable acceptance throughout the more recent literature.

A valuable account of this form of arhythmia is given by Winkler in a paper to which I have already alluded. <sup>(125)</sup> He assured me that he would almost diagnose neurasthenia from this arhythmia alone if it were well marked. In tracings which he took of the pulse and respiration, showing the influence on them when one's attention is taken up, he found that the curves ran strictly parallel to one another; he also observed that when the frequency of the pulse is raised during mental exertion the difference in the period length is almost completely abolished, while it becomes very marked again during the rest after the mental work, as the pulse becomes correspondingly slower. I might also refer to the observations of Braun and Fuchs <sup>(9)</sup> given in a paper, which is not quite in accordance with our present theoretical knowledge. They too speak of the susceptibility of the vagus centre; they regard this variation as a "neurasthenic pulse phenomenon," and on giving small doses of atropine which paralyses the vagus they observed the arhythmia disappear.

Different authors give different views as to the mechanism by which this phenomenon is produced. The most likely view is that put forward by Wertheimer, Meyer, and others, viz., that there is a certain relation between the respiratory and the vagus centre; they hold that the rhythmical stimulation of the respiratory centre has a rhythmical effect on the vagus in such a way that as the respiratory centre becomes active the tone of the vagus centre is diminished, and when the former is at rest the latter is increased. Spalitta <sup>(106)</sup> has given a different and a really very feasible explanation. He showed that on abolishing sensibility or on paralysing the respiratory muscles the variation in frequency due to respiration ceases; and further, that the connection between the centres lies in a reflex mechanism and not in a pre-established simultaneous action. These are his conclusions:—

(1.) The increase in frequency of the heart, observed during inspiration, is a nervous phenomenon of reflex nature.

(2.) The centrifugal fibres are in the vagus nerves, and the centripetal in the nerves of the muscle sense.

(3.) When the inspiratory muscles contract they send out stimuli, which have an inhibitory effect on the tonic action of the vagi, and therefore increase the rate of the heart.

(4.) This phenomenon is not only of importance for the regulation of the blood-pressure, but it also tends to bring about a more rapid supply of blood to the muscles.

These conclusions, with the exception of the last, contain the proof that it is the inspiration that increases the rate of the heart by inhibiting the vagus centre, and not the expiration that diminishes the rate.

A beautiful example of this variation which is met with in numbers of persons, and particularly in many of the lower animals (*e.g.* the dog), is shown in Fig. 29, Plate VI. The tracing was taken from a youth, 16 years old, who had no organic lesion of the heart, but was very neurasthenic and had a strong hereditary taint. This pulse is also a very good example for showing the difficulties which may crop up in analysing regular irregularities, a point to which Lommel also particularly refers. On a superficial examination this tracing looks very like the forms of *allorhythmia* produced by disturbances of conduction. But by carefully measuring the periods, and observing that this variation in rhythm depends entirely on the respiration, one is able to distinguish the two forms with certainty.

It is worthy of notice, however, that there are regular variations of frequency, that have a great similarity to those in Fig. 29, continue for much longer periods, and therefore cannot be due to the respiration. Examples of this variety are given in Figs. 30 and 31, Plate VI. In the case of Fig. 30, I have proved that the rhythm had no connection with the respiration; when a long and short period are measured, some are found to last for eight seconds and more, which would not correspond with a respiration rate of less than 8 per minute. Fig. 31 shows even more conclusively that the variation is quite independent of the respiration; the periods usually last 15 to 17 seconds. In both these tracings it is remarkable that it is the slowing of the heart that always occurs suddenly and appears to come back slowly to the quicker rate. I am therefore inclined to think that there is a periodic inhibition in these cases rather than a periodic increase of the rate. It is, however, impossible to prove this in these cases. I would also observe that Mackenzie, who gives examples of respiratory variations in his

book on the pulse, also remarks that these variations may be more or less independent of the respiration.

§ 59. **Bathmotropic, Inotropic and Dromotropic Nerve Influences.**—Chronotropic nerve influences, as we have seen, can frequently be observed in man; but it is more difficult to detect similar influences on the other properties of cardiac muscle. A disturbance of each property by itself might be detected from its own particular signs, but when the various disturbances occur together and blend with one another, as one would expect from the action of the nervous system, it is necessarily impossible to analyse a case successfully. In many cases, however, it is possible to interpret the numerous points which they show, at least, in some measure. In these cases we would also assume that some nerve influence was at work when the irregularities occurred in paroxysms. In such paroxysms we are bound to exclude any chronotropic influence when the original frequency of the heart at the ostia venosa remains the same, *i.e.* when the frequency is  $\frac{1}{2}$ ,  $\frac{1}{3}$ , and so on. Under these and other circumstances dromotropic and inotropic influences may show themselves by their effect in the form of heart-block. There can be no doubt that in many cases of paroxysmal bradycardia, or, as it is called, Adams-Stokes' disease, the attacks are caused by heart-block through nerve influence. Their paroxysmal character and the distinct signs of interference on the part of the central nervous system accompanying them are strong proof of this fact. And most of the more recent literature on Adams-Stokes' disease agree on this point; at the same time they also go to show that all cases of this disease are not due to heart-block, but very frequently the original rhythm of the heart is really considerably reduced.

This variety of form, and the mechanism of these attacks, is quite conceivable when we consider the extraordinary variety of the effects that can be produced by evidently the same stimulation of certain organs. At one time this disturbance predominates, at another time that; sometimes this combination of disturbances is met with, sometimes another. It cannot surprise us, therefore, that direct or reflex stimulation of certain nerve centres in different persons, and in the same person with a stimulus of different intensity, produces quite different effects.

As yet, however, hardly any attempt has been made to analyse these paroxysmal irregularities with the aid of the experimental

knowledge that has been recently acquired, and yet a fuller insight into the phenomena and their causes can only be obtained by a thorough study of these forms. But as this insight is of great importance from a diagnostic as well as therapeutic point of view, I will here give a few examples taken from my own experience and from the literature, and attempt to give an interpretation of them. And as it is only an attempt, I have had to forego all claim to giving a complete survey of the literature. Besides the authors mentioned in § 35, I would also mention the most recent papers of Jaquet,<sup>(60)</sup> Lewy,<sup>(60)</sup> and Luce.<sup>(73)</sup>

§ 60. **Paroxysmal Bradycardia.** — Fig. 32 (Plate VI.) was taken from a tracing that I received from my friend C. Winkler of Amsterdam. The tracing was obtained on 8th November 1898 from a patient who was suffering from a serious cerebral disease as well as from aortic incompetence. This valvular lesion is the cause of the extremely quick rise and rapid fall of the pulse-wave. Now and then the patient had epileptic seizures, during which the rate of the pulse was considerably reduced, as the tracing (in which the time-marker indicates  $\frac{1}{2}$  seconds) shows. Moreover, the pulse was very irregular; the irregularity was independent of the respiration. (In the figure the radial pulse tracing is shown at the top, the time-marker is in the middle, and the respiratory curve at the bottom.) The analysis of this pulse tracing is very difficult without the simultaneous record of the venous pulse and apex beat; nevertheless, the following facts can be made out:—

For a considerable time the length of the period remains fairly constant, varying between 9.5 and 11-fifths of a second, i.e. the rate is about 30 per minute; we find, however, all gradations from 8.5 to 13, the original frequency is never reduced by  $\frac{1}{2}$  or  $\frac{1}{3}$ ; *chronotropic* influences therefore seem also to be at work. A portion of this more or less regular rhythm, which was observed for many minutes, is reproduced on the lower part of Fig. 32 to the right. Then, however, the rate passes into a much slower one. But this transition is not a regular one; the periods are each lengthened by only an approximately equal amount. In this way periods occur more than  $\frac{3}{2}$  seconds long, i.e. over 4 seconds. If the pulse tracing be observed more closely, we find not only smaller waves occurring in these long periods always at a definite interval after the large perceptible wave, but also small beats at almost equal distances from each other. These small beats appear with perfect regularity

and with great distinctness in many of the longer pauses. As was explained in §§ 35 and 36, and proved by Mackenzie, these small beats in the pulse tracing are due to contractions of the auricle; Webster's case, which is referred to again, also shows these auricular contractions in the pulse curve very distinctly. We must therefore assume in this case that there was a more or less regular action of the auricle; in other words, there was a condition of heart-block, but yet not heart-block alone. The first small elevation in the longer pauses is always larger, often a good deal larger, and sometimes a slightly large wave appears in the middle of the pauses. It appears, therefore, as if the ventricle was under some other influence as well, perhaps a strong negative inotropic nerve influence.

When we define more fully the relation between the large pulse-waves and the small rhythmical beats, it is found that the ventricular contractions clash with the auricular in an irregular manner; now and then the ventricular beat (the large pulse-wave) appears to correspond exactly with the auricular (the small wave), but more frequently occurs independently of the rhythm of the auricle. It seems therefore that the ventricle here takes up its own rhythm independently of the auricle, a phenomenon which was so well marked in the cases described by Chauveau and Mackenzie.

The analysis of this case shows that numerous disturbances arise through the influence of the nerves, and most probably chronotropic, dromotropic, bathmotropic, and inotropic influences affect the cardiac functions and produce heart-block and other conditions. As we have said, a tracing of the venous pulse would enable us to make a more thorough and more certain analysis of cases.

Numerous cases of a similar kind are also found in the older literature, and in some instances tracings are also reproduced. As an example of them, I might quote a case of A. Hubert,<sup>(58)</sup> with its accompanying curve (Fig. 9), in which there was marked slowing of the pulse. If we examine this figure carefully, we see small rhythmical elevations just indicated and nothing more during the long pauses. At the same time it is interesting to note that the pulse-beats are exactly twice and three times as slow as before; this is a case of heart-block. The alternation of a high and low frequency in this case, in which there was also Cheyne-Stokes' breathing,

makes it a very interesting example of arrhythmia due to nerve influence.

Webster<sup>(116)</sup> has recently recorded a most valuable case, and illustrated it beautifully by a large series of tracings. The almost endless variation of forms of arrhythmia in the same patient is shown here exceedingly well, especially when individual types can readily be picked out from these different forms. I am unable to reproduce all his large tracings, and must refer the reader to his original article; but I wish to state at once that in this case also there are small rhythmical beats during the long pauses which are caused by contractions of the auricle. In his Figs. 9-14, 29, 31-40 they are very well marked during the pauses, which are often of enormous length. This case, then, does not exhibit here a chronotropic influence, but is one of heart-block.

At other times, however, Webster found a totally different condition in the heart, and took tracings of it. So far as I am aware, no case of a similar disturbance of the heart has ever been described and illustrated, and I therefore take the liberty to reproduce one of Webster's figures, and I do so all the more readily because this figure shows so conclusively how extremely low the action of the heart in man may become, and yet how life can be maintained in spite of it. It also proves that H. E. Hering is wrong in asserting that these disturbances of function could only be observed in experiment but not in man.

I have reproduced this tracing by Webster in Fig. 33 (Plate VI.). Any one who has stimulated the vagus in experiments will at once observe the effect of vagus stimulation in this tracing. The most remarkable feature in it is the increase in the size of the pulse-waves that appears after the long pauses; that is no doubt due to an increase in the size of contraction in the ventricle, and offers the finest example possible of "Bowditch's staircase." Engelmann's beautiful experiments have now shown what is the origin of this pause and of Bowditch's staircase. He showed in the most conclusive manner that there is here a diminution of contractility. Apart from the cause of the long pause, which is most probably due to a negative chronotropic influence, the contractility at the end of it has almost vanished, but increases with every systole, and in this way the increase in the size of the systoles following the pause produces the staircase. The details of these experiments must be sought in the author's original articles.<sup>(26 27)</sup> From the absolute

similarity between the experimental and the clinical forms, I think every one will be persuaded that Webster's case is one of arrest of the heart from the action of the vagus, where the negative inotropic influence is the most prominent symptom. This influence becomes even more marked in some figures, *e.g.* Fig. 33 *a* and *c*, in Webster's case, by the extraordinarily small rhythmical pulse-waves that follow the long pauses.

In this case, then, we find a very pronounced negative inotropic nerve influence, at other times heart-block, which, as we know, is chiefly due to a negative dromotropic influence, and in the case described in § 57 and illustrated in Fig. 28, we saw an example of an exceedingly strong, purely negative chronotropic effect. On comparing these cases with one another, we find that it is really possible to get an insight into the more subtle action of the nervous system on the heart, and that we cannot only prove that a nerve influence is present, but also find out the effect it is producing. As a further attempt in this direction, I shall now give an analysis of some other forms.

#### § 61. Cases of Positive and Negative Nerve Influences combined.

—I had the opportunity of taking tracings from an elderly woman, aged fifty-eight years, for the first time in the summer of 1900, and then observed a very interesting form of arhythmia which occurred in paroxysms (Fig. 34 *a-d*). The patient suffers from arteriosclerosis and shortness of breath, but shows no sign of organic disease of the heart. She had always a great deal of worry and trouble, and is an exceedingly "nervous" person. She has long complained of palpitation, which annoyed her very much, but never led to attacks of giddiness or syncope. Her heart is still capable of a considerable amount of endurance, as is proved by the fact that she recovered from an attack of influenza complicated by pneumonia. When one feels her pulse, one observes short irregular periods from time to time: the pulse at first is gone, and then returns very rapid and slow, and then the normal pulse suddenly reappears. I took tracings of several such attacks.<sup>1</sup>

Fig. 34 *a* (Plate VI.) shows the beginning and end of a long irregular attack. The intermediate part, which is not repro-

<sup>1</sup> The original tracings which I took first were, unfortunately, lost when they were being reproduced for the "Transactions" of the Dutch Congress, 1901.<sup>(12)</sup> I am therefore only able to produce small portions of the tracings as they were published at that time. Tracings which were taken subsequently, in the middle of 1902, were of great value, but they did not show the *long attacks* that were seen in the first ones.

duced, was exactly similar, showing a type of pulse which closely resembled a low pulsus bigeminus (the beginning and end can be seen in the figure), and lasted 30 seconds. The entire attack lasted 40 seconds.

On analysing this attack, which must undoubtedly be attributed to nerve influences, we find a host of interesting points, although we have only the radial tracing before us.

At the commencement the blood-pressure falls, and so does the tracing obviously, because there is an absence of large systoles. But in the sinking line one can observe small elevations follow each other in quick succession. Those in *a* are copied very badly, but can be made out better in other figures, especially in *d*. They do not correspond to auricular systoles, for they possess a totally different form from the small auricular elevations in the figures of Mackenzie and Webster, as well as in Fig. 32 of this book; besides, they are often much larger than in Fig. *b*. These, then, do not point to a condition of heart-block, but they are really small depressed ventricular systoles. They occur usually at a high frequency, much higher than that of the normal pulse. But this higher frequency is not the cause of the systoles being so small at the beginning of the attack, for even when the frequency is not increased the first systoles are very small, as Fig. 34 *e* shows. We have here, therefore, in the first place *a negative inotropic nerve influence*. In the second place, there is almost always a very great increase in the frequency, *i.e. a positive chronotropic influence is here combined with a negative inotropic*. It is at once apparent that the whole of this tracing cannot be explained by the occurrence of extra-systoles, when we find that the frequency may be sometimes less than normal, as in Fig. *b*, and when we closely examine the other figures.

This combination of positive chronotropic and negative inotropic influences is not unknown in physiological experiments as the effect of reflex action on the heart. Plenty of examples of a similar disturbance in the auricle are given in Engelmann's figures 15, 16, 17, and 20.<sup>(24)</sup> Now these two influences remain distinct throughout the whole attack; the frequency continues increased, the height of the pulse-waves, *i.e. the size of the contractions*, keeps very low. At the same time a remarkable form of allorhythmia is developed; it does not always go on with perfect regularity, but it is characterised by the fact that the small beats occur in pairs. The cause

of this I have not been able to find out. Whether it is an example of real bigeminy of the heart (*cf.* § 21 and § 68), or whether every third beat falls out (perhaps from a disturbance in the stimulus-conduction), or whether it is the combined action of the two nerve influences that produces this effect I cannot say. It is certainly not due to extra-systoles; if it were one should expect every first systole to be normal in size; and, moreover, the big wave often follows the little, as is seen in Fig. *b* and *f*; the ventricle undoubtedly remains in a "hypodynamic" condition, but yet the difference in the periods is too great for a *pulsus alternans* (*cf.* §§ 40, 41).

Now the end of the attack, as shown in Fig. *a* and *e*, is also of especial interest. The blood-pressure, which had kept very low throughout the whole attack owing to the very small systoles, suddenly rises to its normal height, and with this rise the heart returns again suddenly to its normal rhythm; it seems as if the stimulation of the nerve suddenly ceased, and with it the chronotropic and inotropic influences. A small irregularity still appears at times, and the first normal period is frequently slightly prolonged; but these irregularities, when the attack does not occur again immediately, are quite insignificant. That it is really due to an abolition of the negative inotropic influences, and not to negative chronotropic influences, that the contractions are restored to their normal height, is evident from many tracings, *e.g.* Fig. *e*, where, after a very short period of  $\frac{1}{4}$  sec. the pulse-wave suddenly returns to its normal height, after periods of  $\frac{1}{2}$  sec. had previously been followed by quite small waves.

Although the analysis of this case is still far from being complete, it is yet of considerable importance in other respects, and is sufficient to show from the occurrence of very short ill-developed attacks what effect weaker nerve-influences can have on the heart, and hence to offer some points by which to compare other cases.

These short, often almost imperceptible, attacks occurred not only in the first batch of tracings (Fig. *c* and *d*), but constantly in the second (Fig. *f*-*j*), while long fully-developed attacks were never once seen. A thorough examination of these tracings, to which I could add many others of a similar kind, gives one a better notion than a long description would as to how the symptoms of the attack, as above specified, the positive chronotropic and the negative inotropic influence, invariably show themselves. At one time the one influence predominates, at another time the other. The

positive chronotropic effect is especially well marked in Fig. *d*, *f*, and *g*; it is usually most marked at the beginning of an attack. Different combinations of these influences and differences in the course of their action give rise to very different forms. But I would like to draw special attention to those cases in which the attack is merely indicated, as in Fig. *c* and *i*. Although fully-developed attacks, such as occurred in this patient, are extremely rare, the ill-developed forms are not at all uncommon, and the complete attacks which are here given may be of use in the interpretation of similar cases. Thus we saw in Fig. 27 (*cf.* § 57) how a very small negative inotropic effect showed itself alongside the chronotropic.

The ill-developed attacks offer also points of comparison with another class of irregularities. One frequently meets with pulse-waves (*e.g.* in Fig. *c*, *d*, *f*, *g*, *h*), which strongly remind one of bigemini, or intermissions produced by extra-systoles. On the other hand, in cases where extra-systoles obviously occur, but are also accompanied by chronotropic or inotropic effects, we will have to ask ourselves whether they are extra-systoles at all, or there is perhaps only a nerve influence. These cases are more common than might perhaps be expected. A few examples shall be given in the following paragraph.

§ 61 *a*. **Nerve Influence combined with Extra-systoles.**—In § 18 it was observed that with an irregular rhythm of the heart the length of the compensatory pause is not a regular one, and cannot be so, because the original rhythm of the veins is disturbed. But at times the extra-systoles occur so irregularly that one is bound to infer that a definite nerve influence is also at work. This, then, brings us face to face with a question of great clinical importance, whether the disturbance is due to extra-systoles, *i.e.* is of "myogenic" origin, or whether the nerve influence is the chief factor, *i.e.* the disturbance is of "neurogenic" character. This is a question which it is still very difficult to decide, but one which may at least be discussed from concrete examples.

When we look again at Fig. 2 *b*, Plate I, we are at once struck with the great irregularity; the intermissions and the obvious extra-systoles occur without the slightest irregularity or the least regard to the normal rhythm. In another part of the same tracing (Fig. 2 *a*) the extra-systoles occurred quite regularly. In Fig. 2 *b* the small pulse-wave at + cannot at once be taken as an extra-

systole. It may possibly be a systole that is delayed by a negative chronotropic, and perhaps also by a negative dromotropic influence, reduced in size by a negative inotropic effect, but originally produced by a physiological stimulus. But if it is an extra-systole, one is still bound to assume there is also a strong nerve influence at work, considering the extraordinary length of these periods and the great differences in the length of the periods altogether.

The condition found in Fig. 35, Plate VII., is equally remarkable. In this case the compensatory pauses are usually (three times in the figure) too long, in comparison with the preceding pauses. But each extra-systole is followed by a gradual rise in the rate of the pulse, or in other words, by a reduced negative chronotropic effect. Or is it the reverse condition that takes place? Is it that each extra-systole breaks off a rise in the rate of the pulse? This cannot be, because in the regular portions of the tracing the pulse period is usually only  $\frac{2}{3}$  sec. long, and the compensatory pause is followed by a period of  $\frac{2}{3}$  sec.; besides, the slowing of the pulse often begins before the extra-systole occurs. We are bound therefore to assume that the extra-systole is accompanied with a negative chronotropic effect. In physiological experiments examples of this kind are frequently observed, yet the question is whether one can assume a similar condition here. Engelmann (<sup>19</sup> cf. Cushny and Matthews, and H. E. Hering,<sup>40</sup>) states that on stimulating the heart at its base, or in the region of the venæ cavæ, the resultant extra-systole is followed by a few slightly prolonged periods, and he brings forward strong arguments in explaining this phenomenon on the ground that the fibres of the vagus that run in the sinus are stimulated at the same time, and they produce the negative chronotropic effect either directly or reflexly. One might be inclined to adopt the same explanation in this case, and consider the abnormal length of the compensatory pause as due to this negative chronotropic effect. Still it is just this long compensatory pause that makes it improbable that the abnormal stimulus arose in the region of the great veins; it would rather lead one to infer that its origin is at some distance from that point, most probably in the ventricle. Must we then assume that the extra-systole is connected with the negative chronotropic influence in some other way? This is very probable, especially since the slowing of the pulse begins before the extra-systole; all kinds of theories may be put forward,

but nothing certain can be said, and we will therefore have to wait for the results of future experimental research.

Chronotropic changes of the pulse are not infrequently connected with the occurrence of extra-systoles. In the case from which Fig. 36 (Plate VII.) was taken this could often be observed; but in order not to have too many tracings to reproduce, I have restricted myself to one example of this condition (Fig. 36). There we find another peculiarity in the extra-systoles, which raises the question whether there is some nerve influence at work. Two intermissions always occur after each other, with two beats between them. No extra pulse-wave can be seen in the sphygmogram, but on auscultating the heart one can hear the sounds of a contraction every time. With the first intermission, the length of which is regulated by the compensatory pause, a negative chronotropic influence invariably shows itself; this intermission is usually considerably lengthened, and, as in the previous cases, this negative chronotropic influence frequently begins before the extra-systole. This intermission is followed by a large post-compensatory pulse-wave, then a smaller one, and after it the second intermission, which is generally a little too short instead of being too long, and is also accompanied by extra cardiac sounds. Here again we are confronted with the question whether they are real extra-systoles to which a negative chronotropic nerve influence is superadded, or whether it is a primary nerve influence which also gives rise to extra-systoles in some indirect way. Seeing that these systoles occur always in pairs and in the same order, I would rather be inclined to accept the second view, and to compare these disturbances of rhythm in a very general way with the ill-developed attacks in the cases we discussed in § 61 (Fig. 34 c-i).

In conclusion, it is worth noticing that the three patients whose pulse tracings we have been considering in this paragraph were all very nervous, neurasthenic individuals; in the third case the mitral valve was perhaps affected, but in all these patients the "irritable weakness" of the heart was the cause of their cardiac symptoms. This fact certainly corresponds well with a primary nerve influence. Still it is not yet possible to say so with certainty.

§ 62. **The Significance of Nervous Disturbances.**—It was distinctly stated in § 55 that I regarded the analysis of some nerve influences on the heart, which has just been given, merely in the

light of an experiment. It is proved beyond doubt by these cases that we are still ignorant of many factors which combine to produce certain forms, and that it is impossible to get a full insight into the action of the whole heart from a pulse tracing alone. Nevertheless it has been possible (1) to demonstrate the presence of nerve influences in some cases with certainty; (2) to determine the most important influences on the properties of the cardiac muscle in each case; and (3) to obtain, particularly in the ill-developed attacks of nerve influence, some points to guide us in the analysis of other disturbances of rhythm. When several observers take up the analysis of the forms of arhythmia due to nerve influence which are met with clinically, and at the same time take up the analysis of the venous and liver pulse and cardiogram, as Mackenzie has done in such a masterly way, a method which I have been unable as yet to employ in my cases, I am confident that the action of the nerves on the heart will very soon be made clear to us.

The importance of these facts for clinical diagnosis and for treatment must not be under-estimated. The question whether in any given case we have to deal with a disease of the cardiac muscle or a nervous influence is one of the highest importance. Many a patient has had to give up his vocation, or abstain from another, because he was told he suffered from a cardiac lesion, when the cause of his symptoms was purely nervous. On the other hand, many a one has not paid sufficient regard to a serious disturbance of function by diagnosing it a neurosis. And it need not be more than mentioned that our treatment is bound to be quite different in the two cases, and often indeed exactly opposite. The question whether a nerve influence is present or not is therefore one of direct practical importance.

When once a nerve influence has been proved to exist, it is necessary to find out the origin of it. It may either be in the peripheral nerves or in the central nervous system. In practice we have to reckon, in the first place, with general *neurasthenia*. In this condition nerve effects are much more easily produced than normally, and hence reflex influences arising in the periphery or in the psychical centres are much more common.

Still reflex influences on the heart may come from all possible organs, even apart from neurasthenia, from the heart itself, as the experiments of Muskens<sup>(\*)</sup> show (and possibly the case of Luce (*loc. cit.*) might be explained in this way), as well as from the skin,

intestines, &c. That this form of influence on the heart is of the highest significance may be inferred from the fact that the most of the changes in the heart's action, induced *experimentally*, are brought about in this way.

It may happen, however, that both the cortical centres and those situated in the medulla oblongata that control the heart are diseased, or directly stimulated in some abnormal way. We will have to assume such a cause, particularly in those cases where several symptoms of some lesion in the central nervous system occur simultaneously with the changes in the pulse. These would include most of the paroxysmal cases of Adams-Stokes' disease, in which epileptiform and apoplectiform symptoms are most prominent. We cannot go into this question fully here, as it is a purely neurological one. But there can be no doubt that the slowing of the pulse is produced by nerve influence. Webster,<sup>(1)</sup> who discusses this question fully, believes "that the irregularity of the heart is the primary factor, and that the epileptiform seizures are produced by the cerebral anæmia consequent on the suspended action of the heart." It cannot be denied that a very great degree of anæmia must inevitably result from so serious a disturbance of the heart as is found in Adams-Stokes' disease, and it is indeed highly probable that the cerebral anæmia produces the unconsciousness and perhaps some of the symptoms of irritation during the paroxysm. But that does not exclude the fact that the irregularity itself is undoubtedly caused by nerve influence; it may really owe its origin to some pathological condition in the central nervous system, as many of the cases recorded show; there may be possibly no visible sign of a lesion there post mortem, but that does not prove that the centre involved, usually the vagus centre, was not abnormally stimulated either by some central changes which cannot be detected anatomically or by some reflex channel.<sup>1</sup> But here also there is a great field for research, physiological as well as clinical.

<sup>1</sup> N. Ortner (Volkmann's *Vorträge*, No. 347) has recently compared the cases of Adams-Stokes' disease with the "claudication intermittente," and has termed them "dyspragia intermittens angiosclerotica cerebialis (medullaris)." Intermittent spasm of the vessels can certainly, I think, be regarded as a cause in these cases.

## CHAPTER III

### CLINICAL TYPES OF ARHYTHMIA

§ 63. **Necessity of a Revision of the Clinical Nomenclature.**—The facts which we have obtained from physiology towards an explanation of the irregularities of the heart will form the ground-work on which the future study of these irregularities must be based, and will be bound to lead to a better classification and a logical nomenclature for the various clinical forms of arhythmia. In clinical work, where it is more and more evident that totally different conditions are included under one name, men recognise more and more the necessity of testing old names and distinctions by our present knowledge, and of revising and improving them. There is no better means of creating confusion and misunderstanding than the use of wrong names and designations. When it was found indispensable in other branches of science to institute a proper terminology, a similar claim for clinical medicine, wherever so many obsolete words are still employed, cannot be refused.<sup>1</sup>

In this chapter we shall endeavour to throw some light on the antiquated, meaningless, or even wrong names for the various forms of arhythmia. This can be no more than an attempt as yet, for it will take many years' work by numerous observers before all the problems in arhythmia can be solved. Still it is absolutely necessary to take up the work, and I trust that what is done here will help a little towards their solution. I make no claim for completeness; there are too many cases demanding a complete explanation for that; there are still too many types of pulse which I am completely at a loss to explain. Nevertheless we can only make practical use of what has already been discovered, when a proper clinical nomenclature has been drawn up.

<sup>1</sup> In view of this legitimate claim, it is really surprising to read in an article by L. Bard (*Semaine médicale*, 15th April 1903), in which he quotes the work of W. His, jun., and myself, that they "ont un grave défaut, celui de séparer ce que la clinique réunit, de ordier des différences de nature et d'espèce, là où il ne paraît exister que des différences d'intensité et de degré." When two conditions have been proved to be absolutely different from one another, and this proof is rejected on the ground of their superficial clinical resemblance, then all scientific work is at an end! It is just because there are conditions really different, which may look like each other, that this distinction is so absolutely necessary!

In making this demand I would point to Ludwig Traube himself, who emphasised the connection between clinical medicine and physiology more than any one else, who, while he was a clinician, always sought for an explanation of the conditions which he met with in physiology and in experiment, and who was the founder of the modern clinical ideas with regard to the pathology of the heart. Is it surprising that many of the explanations which Traube gave for pathological conditions in the heart hold good no longer? Certainly, no one would rejoice more over the advance that has been made in the physiology of the heart, and has given us a much deeper insight into the action of this important organ, than Traube himself. We are surely following out his aim when we try to adapt our clinical notions to modern knowledge.

#### PULSUS IRREGULARIS

§ 64. **Arhythmia and Pararhythmia.**—The name “pulsus irregularis,” or irregular pulse, is a useful one as a collective name for all possible irregularities of the heart and pulse. At the same time we must bear in mind that this “irregularity” does not always bear the same significance, because it can be produced by very different causes. Even the degree of irregularity that is observed in the heart or pulse is no gauge of its pathological importance; for the normal rhythm of the heart is frequently totally obscured by extra-systoles without any injurious result, while the most serious cardiac diseases often exhibit a pulse that remains regular up to the very last.

The name pulsus irregularis is still employed in a certain sense, viz., in contradistinction to “pulsus inæqualis.” In this sense it denotes an irregularity in the length of the periods and true arhythmia. But here we might readily fall into error, for differences in the period-length can be brought about by very different influences. We must bear in mind that irregularity of the period-length can occur in the following forms:—

1. With preservation of the regular rhythm of the heart (pararhythmia).

- a. In a more or less regular manner from extra-systoles.
- b. In the form of allorhythmia of various kinds, such as those we saw arising from a disturbance of conduction, contractility and excitability.

## 2. With a change in the rhythm of the heart—

a. At definite times, *e.g.* the variations in the period-length due to respiration.

b. In a perfectly irregular manner.

It is therefore distinctly desirable, even when the term *pulsus irregularis* is used to denote a pulse with unequal periods, to distinguish between the various forms here named which differ entirely in their origin.

## PULSUS INÆQUALIS

§ 65. **Unequal Height of Systoles.**—When a pulse shows beats of unequal height, we speak of *pulsus inæqualis*. But this name does not have one special meaning, as it is employed for various types of pulse.

The size and height of a pulse-wave depend, *ceteris paribus*, on the contractility of the ventricular muscle, on the degree to which the ventricle is filled, and on the amount of blood in the artery in which the pulse is observed, &c. The contractility and the degree to which the heart is filled, are less, the shorter the interval between the contractions. It is thus quite evident that within certain limits every change in the period-length causes a change in the height of the waves; after a long pause (*e.g.* the compensatory) the wave will appear larger, after a short pause smaller. So, too, considerable inequality in the pulse is observed in true arhythmia (*e.g.* in Fig. 5 and c) as well as with extra-systoles, as the result of the difference in the length of the period.

The inequality of the pulse-wave is of greater importance when the rhythm is a regular one, or where small pulse-waves occur after a long pause. In *pulsus alternans* the contractions are rhythmical in time but unequal in size; this is a case of real *pulsus inæqualis*. An example of the second kind is found in those cases which were described in § 61 and illustrated in Figs. 26, 27, 34, where, as a consequence of a negative inotropic nerve influence, the height of the waves was less in spite of longer or equally long pauses.

Finally, the *pulsus paradoxus*, in which the pulse becomes smaller or disappears entirely during inspiration, is a true unequal pulse; but the cause of it is not in the heart itself, the force of which is not directly affected.

We cannot therefore be content with establishing the presence of an unequal pulse, but we must endeavour to find out the nature and cause of it in each case.

#### PULSUS BIGEMINUS AND ALLIED FORMS

§ 66. **The Analysis of Pulsus Bigeminus is urgently required.**—The type of pulse which has been most studied, most described, and led to most controversy, is undoubtedly the pulsus bigeminus, so called. This term has long been used to designate the occurrence of two systoles in quick succession, followed by a long pause. It is at once obvious that it is an altogether unsatisfactory term, because this phenomenon may arise in very different ways. It gave rise to controversies all the more readily because men also spoke of bigeminus of the heart, or “cor bigeminum,” and different authors put a different construction upon this condition which was able to produce the picture of a pulsus bigeminus. It had long been my intention to find out the various causes of so-called pulsus bigeminus, and to determine its relation to the condition of cor bigeminum which perhaps also occurs in man.

In the first article which H. E. Hering wrote on the analysis of irregularities of the heart <sup>(40)</sup> he expressed his astonishment that I contemplated making a research into pulsus bigeminus, because in demonstrating the occurrence of extra-systoles in man I had already unconsciously analysed the bigeminal pulse. He referred to this point again and again, and F. Kraus, <sup>(64)</sup> evidently without fully considering the matter, recently expressed the same opinion as Hering, that I had analysed the pulsus bigeminus without knowing it. Hering's astonishment that I still wished to take up the analysis of this type of pulse, is, I must confess, quite as inexplicable to me, for nothing is more clear than that very different types of pulse are still included under this name. Hering's own articles show in the plainest possible manner how many mistakes can arise from a term that is wrongly employed or ill chosen.

It is, however, quite certain that more recent observers have made the same error in putting so much weight on the name pulsus bigeminus, and it is a very easy matter to prove (1) that this name, as it is now employed by Hering and others for the appearance of extra-systoles, is in itself incorrect, indeed absurd; (2) that on historical as well as logical considerations, this name must be

reserved for a few rare cases; (3) that it has frequently given rise, and still gives rise, to a wrong interpretation of pulse irregularities, that very different forms come under its definition, that it can only cause confusion, and therefore must be dropped and replaced by better names.

§ 67. **The name Pulsus Bigeminus has no Meaning.**—As regards (1) the researches, which were quoted on the part which extra-systoles play in man, go to show that in almost all cases where the term *pulsus bigeminus* is used, *i.e.* where two pulse-beats follow in quick succession and are followed by a long pause, the second systole is an extra-systole in the physiological sense. Now, Hering's experience was limited to this form, and so he at once assumed that this was always so. But if it were, this very fact would be a very strong argument for the need of another term for this phenomenon, for the following reasons:—

An extra-systole is produced not by a physiological stimulus, but by an abnormal or extra stimulus affecting the cardiac muscle, which is often over-excitabile. This stimulus affects the heart at the ventricle, auricle, or in the region of the ostia venosa; in other words, not at the point where the normal stimulus acts. The extra-systole is therefore different in origin from the physiological systole, and has also a totally different course when it starts in the ventricle or auricle (*cf.* § 25). It is not surprising that the two systoles coming quickly after one another were formerly regarded as allied to the "two-peaked waves" observed by Traube in his case of bigeminy of the heart. But now it is not desirable, either on practical or on theoretical grounds, to call this type of pulse a bigeminal pulse when we know that the second systole is an extra-systole. And all who see how unsuitable this term is, and desire that in clinical medicine an idea and the name which it bears should correspond as far as possible, will, I trust, agree with me when I propose to use the term extra-systole here and not *pulsus bigeminus*. I almost believe Traube himself would not have wished otherwise.

§ 68. **There is a true Bigeminy of the Heart.**—As regards the second point which we raised, it is certainly no light matter to drop an old name without good reason, because such a name possesses an historical value. Apart from my reasons for thinking that it should be dropped, I must emphatically say that the name *pulsus bigeminus* has absolutely no historical value, that it was wrongly

employed from the very beginning, and that the clinical phenomenon was compared with an experimental result that did not correspond with it.

Traube<sup>(111)</sup> was the first to describe "two-peaked waves," which he observed in his experiments under certain conditions. He speaks of them in his *Gesammelte Beiträge* for the first time in page 315, where he states that the two-peaked waves "correspond with two distinctly perceptible beats in the intact crural arteries." On pages 296, 326, 373, he demonstrates that they are not dicrotic waves; in dicrotic waves there are two waves to one systole, but with these waves there are two systoles with quite distinct cardiac sounds. He first speaks of "pulsus bigeminus" on page 448 when, the rate of the pulse being extremely slow (from digitalis, nicotine, potassium cyanide, carbonic acid, carbonate of soda), the two vagi are cut. The best example of his two-peaked waves, the bigeminy of the heart, is found in his Fig. c, Plate 9.

In a subsequent article<sup>(112)</sup> Traube attempted to apply the results of his experiments to clinical symptoms, and stated that he had observed a pulsus bigeminus in some very bad cases, which he put down to "two-peaked waves"; then he described a special variety of pulsus bigeminus which he calls pulsus alternans: this case, which we have already fully discussed, was the first one of pulsus alternans described (*cf.* § 42). In it the small wave was somewhat retarded, and he therefore speaks of a variety of pulsus bigeminus, because the bigeminus, according to his notion (p. 221), consists in this, "that every two pulse-waves that occur in the arterial system are followed by a long pause."

At that time Traube was perfectly justified in making this definition and comparing these different types of pulse; now, however, we know that this term is no longer applicable to the phenomenon which Traube studied. Still, physiologists as well as clinicians have extended the use of Traube's term and the idea of "bigeminus" more and more.

Knoll<sup>(62)</sup> has made a great contribution to the expansion of our knowledge by his exhaustive and excellent researches; he proved that the length of the bigemini was often exactly twice or three times as long as the normal period. Heidenhain,<sup>(38)</sup> Böhm,<sup>(6)</sup> Stricker,<sup>(110)</sup> Fraentzel,<sup>(31, 32)</sup> Tschirjew,<sup>(113)</sup> Sommerbrodt,<sup>(104)</sup> Riegel in his numerous valuable contributions,<sup>(92-94)</sup> Rosenstein,<sup>(97)</sup> and many others, showed, in contradiction to Traube, that no grave

significance is to be attached to the bigeminal pulse, and that this type of pulse can very often be observed, at least in the form of isolated bigemini, here and there. Now, all these observers had almost exclusively looked for "two pulse-waves that are followed by a long pause," the second of these two being, as we now know, an extra-systole.

I had just taken up the study of this form of pulse irregularity when it became clear to me that all the controversies among various authors arose from two facts: (1) that nothing was known of the causes of the irregularity of the heart, and consequently of the various causes of "two pulse-waves followed by a long pause"; and (2) the pulse phenomenon was compared with an experimental one which did not correspond with it (as was, of course, also done by Traube himself in the case of *pulsus alternans*). For in the first place, as Traube's own illustrations and words bear out, he conceived a continual bigeminy ("every two beats followed by a long pause"), while in the second place, the condition which Traube called by the name of "two-peaked waves" has obviously no connection with extra-systoles at all!

When Traube's figures, and more especially Fig. *C* (Plate 9), which he himself calls the best, are thoroughly examined, it is found that the contractions, which occur in pairs, are not followed by a compensatory pause; these pairs, then, correspond, not to a normal systole and an extra-systole, but to one systole of the heart. There is here a doubling of the heart-beat, a real bigeminy of the heart. At the same time we do not say that in other experiments, particularly in Knoll's, they are not extra-systoles; yet Knoll explicitly states that the bigeminus corresponds to two or three normal systoles, a fact which probably (it would be better to say "perhaps") points to extra-systoles. The bigeminy of the heart, as described by Traube, however, is certainly not due to extra-systoles, at least it is most improbable; this fact constitutes a very great difference between it and other clinical types of pulse that were subsequently described.

It is not surprising that no notice was formerly taken of this fact; but very few would think of real extra-systoles in Fig. *C*. of Traube on looking at it now. It seems to me that Tschirjew observed this fact, although he employed it incorrectly by denying the occurrence of premature systoles in bigeminy, and regarding the second pulse-wave as a dicrotic one. But Rosenstein, who worked at these pulse forms in the seventies, wrote to me a long

time ago that the *pulsus bigeminus*, so-called, was in his opinion incorrectly applied to Traube's two-peaked waves, as Traube had described something quite different.

We must, therefore, really assume that two different conditions were confounded in experiment as well, and we can now but hope that these questions will be again investigated experimentally, as H. E. Hering and others have done, careful attention being paid to the differentiation of true bigeminy of the heart from extra-systoles as far as possible.

The question now arises whether a true bigeminy, or twin contraction of the heart such as Traube observed, also occurs and can be demonstrated in man. I certainly believe it can, and this is my main reason for thinking that it was absolutely necessary to give a separate description of the conditions which are included under the name *pulsus bigeminus*.

When an artificial stimulus is applied to the mouths of the great veins and an extra-systole is set up from that point, it is not followed by a compensatory pause, but by the next physiological systole after the normal interval (for the explanation of this *cf.* § 16). If now extra-systoles proceeding from the veins should occur in man, we would in most cases be unable to say with certainty whether the contractions were extra-systoles or premature physiological systoles (*cf.* §§ 16, 77-83), because when there is no compensatory pause we thereby lose the sure sign of an extra-systole. If the rhythm is otherwise perfectly regular, we may assume that we have to deal with extra-systoles, even when the pause is very small or absent altogether; if, on the other hand, the rhythm itself is irregular, we are unable to say whether it is the one or the other (as in Fig. 5).

But there are cases (briefly alluded to in § 21) in which a totally different condition is found; in them every systole is followed by another for a considerable time, although this second systole is not followed by a pause but by the normal interval; and, in spite of any irregularity of the rhythm, the systoles that occur in pairs invariably appear in exactly the same order, the interval between them remaining constant to within .01 sec. In the cases where the systoles occur in pairs we have no longer a right to assume that they are extra-systoles; we must first think of Traube's bigeminy.

Let us look at Figs. 8 and 9, Plate II. In Fig. 8 *a* we find

(§ 21) an irregular pulse, in which certain variations in the irregularity can be observed. When bigeminy of the heart continued for a considerable time, the second systole always occurred exactly at the same interval after the first, as we see in Fig. 8 *b*; they do not once occur in any other order. But the second systole is never followed by a pause, but only by the normal period, which exhibited exactly the same variations in length as when there was no bigeminy. The contrast between the irregular pulse and the regular occurrence of the second wave is very striking.

The same condition appears in Fig. 9, as is verified by the cardiogram. We will not enter into other questions bearing on the slow rate of this pulse, but would call attention to the bigeminy of the heart. There was not the slightest sign of a pause in this case either; the two systoles were apparently closely connected with each other, while extra-systoles never occurred once during the long pauses between the single systoles. I took a large number of tracings of this bigeminy, and invariably found the same sequence in the pairs of systoles. I thought it would be of interest to show here the transition from the bigeminal action to the single beats of the heart.

Cases of this kind, I think, are not extremely rare, but form a very considerable proportion of the cases of so-called "regular pulsus bigeminus." In my paper before the Eighth Medical Congress I expressed the opinion that probably 95 per cent. of the cases of so-called pulsus bigeminus were due to extra-systoles. But how many of the remaining 5 per cent. are cases of true bigeminy I am unable to decide. It must, however, be distinctly stated that in attempting to analyse these types of pulse, attention must be paid to the presence or absence of a compensatory pause, and to the length of the interval between the pairs of systoles. If several observers would take up this point a solution to this problem would no doubt be found.

The question naturally arises, What is the mechanism that produces this bigeminy of the heart? We must wait for an answer from physiologists; it seems to me a very interesting problem. It is impossible to entertain seriously the idea of a prolonged peristalsis of the ventricular muscle, as Tschirjew and others have proposed, a contraction at two different rates; moreover, it is quite apparent that there are really two systoles (*cf.* Fig. 9 and also Traube, *loc. cit.*). The simplest explanation to give would be that

in these cases the contraction-stimulus lasts so long that, even after the systole has begun and ended, the stimulation continues until the irritability of the cardiac muscle returns, and another systole is at once excited. When the length of the refractory phase and the intensity of the stimulus in a regularly acting heart are fairly constant, it would easily explain why the second systole must always follow after a constant interval.

We cannot, however, accept such a ready explanation as that off-hand. In Chapter I. (§§ 3, 51), it was argued that all facts point to the theory that the contraction-stimulus, the stimulus-matter, is destroyed by the contraction of the muscle-cells, and after the systole is built up anew to an effective intensity. The stimulus therefore cannot last beyond the systole, except under very special circumstances. This might happen if a number of the muscle-cells, that produce the stimuli, did not contract; if a part of the musculature round the ostia venosa is for some reason less irritable, this part will not contract when a systole begins, but the stimulus-matter in it will go on accumulating till it reach a greater intensity; and after the systole is past it will perhaps be able to excite another whenever the excitability of the heart is again sufficiently restored. The continuance of the stimulus-production in certain parts of the heart might arise in another way, viz., that through the arrest of conduction at one part that part did not contract with the first systole, but became the starting-point of the second. The results of Muskens' <sup>(34)</sup> experiments seem to point to the possibility of some such condition; he found that a dissociation of different parts of the muscle fibres may arise just at the root of the frog's heart. This dissociation appeared when the heart was placed in a certain position, and was probably the result of stretching or of diminished blood-supply to certain parts of the muscle. In reference to this condition it is deserving of notice that, in the two cases which I have here described as well as in others which I have observed, the bigeminy was wont to come and go on changing the position of the body. I will, however, refrain from going further into these purely speculative problems; we must leave them to the physiologist to settle.

When one auscultates a heart showing bigeminal action, one gets the impression that each systole is itself the cause of the second one. One might then ask whether the first systole does not actually supply a new contraction-stimulus, say by the traction

of fibrous pericarditic adhesions or by changes in the endocardium. If this were so, it would be an unusual kind of extra-stimulus. On the other hand, the second systole would be bound to produce a third, and in cases such as those here described the stimulus would have to act at the mouths of the great veins, because there is absolutely no compensatory pause.

Although no sound explanation has yet been given of this phenomenon, the proof that this form of bigeminy of the heart does occur in man is sufficient to make us assert that it is only in this condition that we can speak of bigeminy of the heart in Traube's meaning, and that the name bigeminy of the heart for this phenomenon is alike logical and historically sound.

The term "false bigeminy" might be employed for those cases in which extra-systoles assume the appearance of a bigeminy. But it was argued in § 67 that this term is an absurd one; and it will be shown subsequently that it is clinically incorrect, and gives rise to gross mistakes.<sup>1</sup>

§ 69. **The name Pulsus Bigeminus is misleading.**—It remains finally to show how the name pulsus bigeminus has very often given rise, and even yet gives rise, to confusion.

In the last paragraph we explained how the notion of Traube's bigeminal action of the heart had been entirely dropped, and was replaced by a condition which was due to extra-systoles. That was the first and fundamental error which was caused by the name pulsus bigeminus and its definition; but it shall now be my endeavour to resuscitate the idea of a real bigeminy of the heart—a condition which I believe I have found in two cases.

The pulsus bigeminus, as usually accepted, appears as two pulse-waves, which succeed each other quickly and are followed by a long pause.

But this description is equally applicable to the alternating action of the heart with an early occurring small wave, and the similarity of these two types on superficial examination is so complete that it is not surprising that a controversy was long waged over the identity of the pulsus bigeminus and pulsus alternans, and even H. E. Hering still refuses to believe there is any difference between these two forms in man. Still, I think I have already proved, in the section on the disturbances of contractility, that a real alternating action of the heart may lead to pulsus alternans

<sup>1</sup> *Vide* Appendix 6.

in man. We must at once admit that *pulsus alternans* can be produced by extra-systoles, and also that the *alternans* which I described is not, as Hering thinks, a *pulsus bigeminus pseudo-alternans*, but a *pulsus alternans pseudo-bigeminus*.

But this form of pulse can also be produced by a disturbance of conduction. In the section dealing with the disturbances of that function, it was proved that a regular intermission of the pulse may arise from that cause. When an intermission occurs after every two beats, we obtain an exact tracing of the *pulsus bigeminus* (cf. Fig. 13, Plate III.; and 17 *b*, Plate IV.). In tracings of this kind in which the intermission occurs more rarely (Figs. 12, 16, 17, 18) we observe the most beautiful examples of *pulsus bi-, tri-, and quadri-geminus*, but where extra-systoles do not occur we cannot speak of a bi- or tri-geminal action of the heart.

But even when we confine ourselves to irregularities due to extra-systoles, mistakes are not avoided, and it is easy to point to large numbers of such errors throughout the literature. I might point, for example, to the works of F. Riegel, and show how he was led by the form of the pulse-tracing to give an entirely erroneous explanation of the tracings he has reproduced.

In Figs. 1 and 2 of his first article on arrhythmia of the heart <sup>(2)</sup> the period from the small pulse-wave to the next large wave is twice as long as that from the large wave to the next small one. This shows most conclusively that this tracing is *not* an example of *pulsus bigeminus*, but that the extra-systole did not occur *till after* the small wave, and did not produce an extra pulse-wave, as very often occurs with an early occurring extra-systole (cf. e.g. Fig. VI., Fig. 6, &c.). An extra-systole follows, therefore, after every *second* systole, not after every systole. The greater fall of the curve during the pause is caused by a smaller amount of blood in the artery after it, and hence the next succeeding wave appears much larger; but yet we know that the post-compensatory systole and its pulse-wave are also greater than normal. The abscissa of the curve does not correspond to the lowest point of it, but is found by joining the bases of the small waves. That this is the right interpretation is proved by Fig. 3, where the extra-systole does produce an extra pulse-wave. In the same volume (p. 506), Riegel gives a tracing of *pulsus alternans duplicatus*. It is obvious that in it an extra-systole occurred after three systoles; the post-compensatory wave is large, the second a little less, the third is of normal height, and then comes the small extra-systole.

A similar explanation may be given of Figs. 7, 14, 17 in a subsequent article of his.<sup>(98)</sup> Figs. 20 and 21 show how impossible it was to draw a correct distinction between *pulsus bigeminus* and *alternans* in this way. Fig. 20 is supposed to be a tracing of the former, and Fig. 21 of the latter. It is seen from Fig. 22 that in both cases the irregularity was caused by extra-systoles.

The same confusion is found in Riegel's last work on arhythmia.<sup>(94)</sup> It is highly improbable that Figs. V. and VI. are true cases of *pulsus alternans*: the change in the rhythm is very possibly the result of a disturbance of conductivity (*cf.* above). If the periods in Figs. VI. and VII. are measured as accurately as possible, it is evident that they show not a *pulsus trigeminus*, nor two extra-systoles occurring after every systole, but one extra-systole coming after every two systoles.

It was previously impossible to give a correct explanation of these forms of pulse, and I have cited these examples only to show how such an experienced clinician, who was continually devoting himself to the study of arhythmia, was misled by the name "*pulsus bigeminus*." And in interpreting the pulse tracings that are reproduced in this book mistakes might easily be made; thus, one might say there was a *pulsus bigeminus* in Fig. 6, Plate II.; but in that case an extra-systole occurred after every two contractions, but did not produce an extra pulse-wave.

Finally, I would point out that *pulsus bigeminus* may be the result of a true arhythmia, the irregular physiological stimulation of the heart, as is seen in Fig. 5, Plate II.

We see, then, that the *pulsus bigeminus* can arise from very different processes in the heart. In Fig. XX., I have endeavoured to set forth these various processes in a diagrammatic form. In this figure ↓ represents the physiological stimulus, ¶ the extra stimulus that sets up an extra-systole. The regular pulse is shown in *a*. In *b* extra-systoles occur, giving rise to the *pulsus bigeminus*. The first two are ventricular extra-systoles; hence the compensatory pause is complete, and the rhythmical stimulation of the heart continues the same; the last two proceed from the auricle in the neighbourhood of the ostia venosa, the compensatory pause is slightly shorter, and hence the next physiological systole occurs a little sooner. (Hering calls this latter form the "*shortened bigeminus*"; a shortened twin cannot be termed an appropriate name for a pulse-phenomenon.) In *c* again there are extra-systoles: in this case it depends whether

the extra-systole produces an extra wave or not, that, as in the first example, a group of beats like pulsus trigeminus, or in the second, a group like a bigeminus occurs at the radial; moreover, this

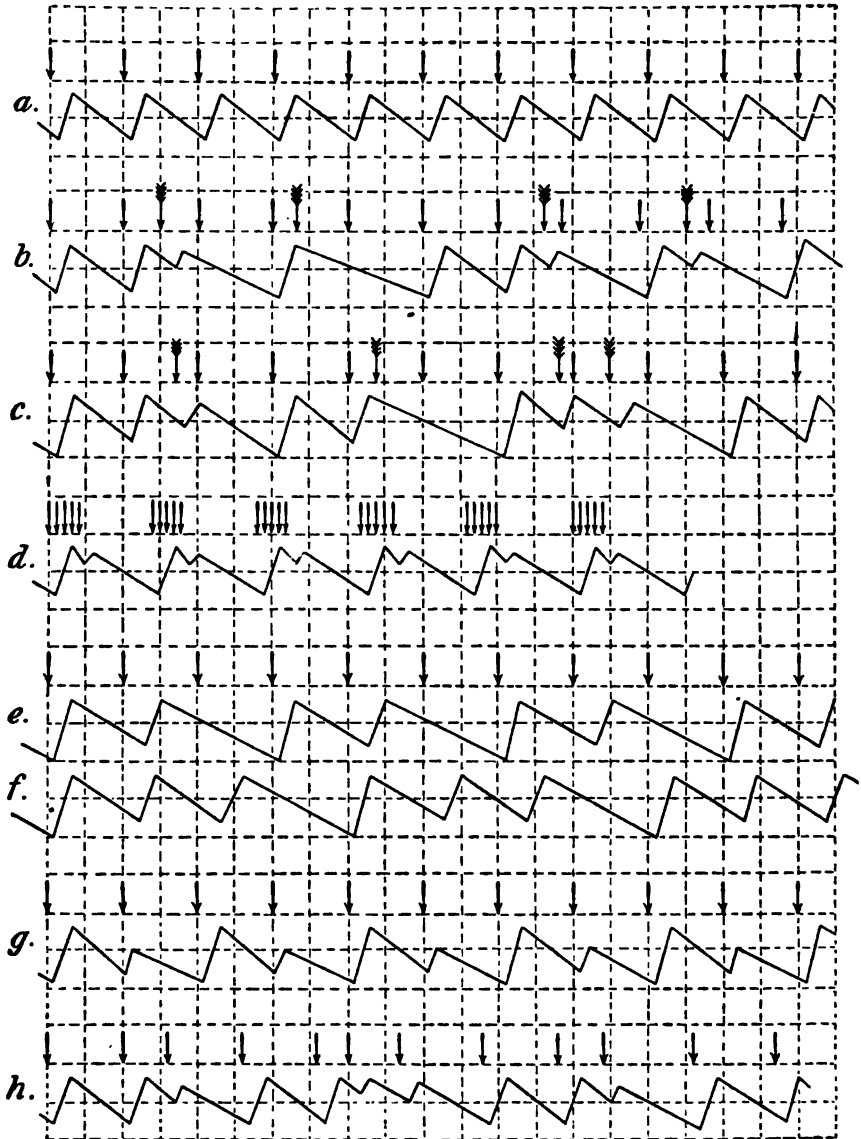


FIG. XX.

figure shows a trigeminy due to the occurrence of two extra-systoles. The true bigeminy of the heart is shown in *d*; in this case one must remember that the second systole may or may not show itself

in the pulse tracing. (In the diagram the cause is supposed to be in the continuance of the stimulus, *cf.* § 68.) *e* and *f* are examples of groups resembling bi- and tri-gemini produced by the dropping out of systoles in consequence of an arrest of conduction. *g* is the pulsus alternans with premature small wave, resembling the pulsus bigeminus; in *h* there occur groups like bi- and tri-gemini due to irregular stimulation at the base of the heart.

It could perhaps be shown that there are other causes for a pulsus bigeminus in the peripheral arteries. But those that have been given will, I think, suffice to show conclusively that the name pulsus bigeminus is no longer appropriate. When my opinion, that there is a real bigeminal action of the heart in Traube's sense, is once accepted, I think a very suitable term for the condition would be *bigeminy of the heart*, or *cor bigeminum*. But we ought no longer to speak of a pulsus bigeminus. The irregularity should be carefully analysed in every case, and designated by a proper name. In most cases it can be shown that extra-systoles are the cause—one should then speak only of extra-systoles. That name is perfectly correct, and is borne out by physiological facts. The name abortive (*frustrane*) systoles is not correct: (1) because there are abortive contractions that are not extra-systoles, and extra-systoles need not always be abortive (*cf.* § 25); and (2) because we know the essential significance of those systoles rests on the fact that they have no part in the normal action of the heart, but are the product of an extra stimulus.

For similar reasons the name "*premature contractions*," as used by Mackenzie (*vorzeitige Systolen*) is unsuitable; these systoles are not premature, like those in Fig. 5, but accidental or additional.

Nor can I accept the name "*myoerethic irregularities*" which Hering introduced. So many different irregularities and varieties of pulse can arise from stimulation and altered excitability of the heart that I cannot see any advantage in this new name.

And it does not require more than mention that the terms pulsus trigeminus and pulsus quadrigeminus must be given up as unsuitable and liable to cause confusion.

I can only regret that more recent writers, such as Hering and Lommel, have again introduced these names for those very cases in which extra-systoles are the cause. When Hering himself very rightly advocates a proper terminology for physiology, he cannot surely reject a reasonable demand to rid our complicated clinical

nomenclature of absurd and confusing names. It was with this aim in view that I thought it absolutely necessary to make a special analysis of the so-called *pulsus bigeminus*.

#### PULSUS INTERMITTENS, DEFICIENS

§ 70. We speak generally of an intermission of the pulse when pulse-beats fall out now and then. Such a condition in the great majority of cases is due to extra-systoles, but it can be produced by various causes. It had been observed that a systole was not always missed when a pulse-wave dropped out, but on the contrary an abortive or weak systole could usually be made out. Those cases, however, in which the systole was also absent, went by the name of *pulsus deficiens*. That is the generally accepted idea, which has been recently emphasised again by Hering.<sup>(48)</sup> F. Kraus has evidently taken up Hering's views in speaking of *pulsus deficiens*, and says in a paper, to which we have already referred, that I have cited cases of *pulsus deficiens* as examples of a regularly intermittent pulse, and have not taken into consideration that there are many possible ways of explaining the *pulsus deficiens*. I cannot understand how Kraus made such a statement, for in my earlier articles I had expressed an opinion on quite definite forms of missed systoles with absolutely definite characteristics, which I ascribed to disturbances of conduction. But as to the causes of other forms, I had not up to that time published any articles in German. Kraus cannot, therefore, know very well what I had, or had not, considered.

If we look at the names for these forms in the light of our present knowledge of physiology, we find there are three causes of *pulsus intermittens* with systole: (1) extra-systoles; (2) early occurring physiological systoles; (3) very small contractions in alternating action of the heart. It is quite clear that the name "*pulsus intermittens*" is not a suitable one for all those cases. The word intermission is generally used of any symptom when that symptom is *not present* at any time, *e.g.* intermittent fever. But here a systole, although an abnormal one, *is* present during the intermission in the pulse; we should therefore employ a proper designation for the symptom in every case, and state the presence of extra-systoles, or of early-occurring or weak contractions. If we merely use the name "*pulsus intermittens*," we do not denote by it what is going on in the heart.

The same objection holds good for the term "pulsus deficiens"; it is, moreover, almost never employed in clinical work, and should be dropped entirely. For it merely denotes that the pulse-beat is absent, while one really means to express the absence of a cardiac systole by it. This absence of the systole now can be caused: (1) by the missing of exactly one contraction as a result of disturbances of the conductivity or excitability; (2) by the absence of the physiological stimulus through a negative chronotropic, or even negative bathmotropic, or dromotropic influence.

In the first case, where a systole drops out frequently at regular intervals, it would be logical to speak of a *pulsus intermittens*, for then there is not only an intermission of the pulse (the missing of exactly one pulse-beat), but also an intermission in the action of the heart by the missing of exactly one systole. In this case, therefore, it would be correct to employ the old and familiar term, *pulsus et cor intermittens*.

In the second case, however, there is no intermission; the frequency of the pulse is for a short period greatly reduced; the pulse is delayed sometimes more and sometimes less. This phenomenon, which I treated of in § 57 and illustrated in Fig. 27 *a* and *b* (Plate V.), has been discussed by numerous authors, *e.g.* Cushny<sup>(43)</sup> and Hoffmann,<sup>(64)</sup> and recently by Hering.<sup>(48)</sup> But it is, I think, incorrect to speak of it as "*pulsus deficiens*." The pulse-wave is not missed, it is only retarded. If, therefore, a name is required for this form of irregularity, it should rather be "*pulsus retardatus*." Still I am inclined to believe that more progress will be made in the study of the irregularities of the heart and pulse if less attention is paid to the name and more to the thing itself.

### PULSUS ALTERNANS

§ 71. After what has been said on *pulsus alternans* in the section on the disturbances of contractility, it is unnecessary to discuss it at any length again. We might just point out that the name *pulsus alternans* should only be used when an alternation of the heart occurs; in this I quite agree with Hering. At the same time, we should bear in mind that there is not only a *pulsus bigeminus pseudo-alternans*, *i.e.* a form of movement of the heart which simulates the *pulsus alternans*, but also a true *pulsus alternans* which, under certain conditions, may resemble a bigeminal pulse, *i.e.* is pseudo-bigeminus.

## HEMI-SYSTOLE

§ 72. By hemi-systole we understand clinically a change in the action of the heart, where the right and left halves do not always work together, either because they beat alternately, or the one or the other half remains at rest now and then, or both contract in different rhythms.

It was long ago shown conclusively that the cases in which hemi-systole was diagnosed were almost all, without exception, cases of extra-systoles or heart-block at the auriculo-ventricular groove. These conditions can quite easily explain the possibility of a venous pulse occurring without an arterial pulse at the same moment (*cf.* the sections on these conditions given above). There is no doubt that hemi-systole is of little or no moment as a clinical symptom of cardiac disease.<sup>1</sup>

It is very improbable that we can go so far as Hering does,<sup>(42)</sup> and assert that at all events hemi-systole cannot possibly occur in man. The results of physiology furnish several facts which indicate that one or more chambers of the heart may now and then fail to contract with the rest. In this connection some significance must certainly be attached to heart-block, which can be observed clinically. It is also remarkable that the right auricle may cease to contract when it is overfilled with blood, as Gerhardt<sup>(36)</sup> and Mackenzie<sup>(75 pp. 186, 285)</sup> have shown. Still this is only a partial, not a true, hemi-systole.

A case of unilateral bradycardia observed by E. Moritz<sup>(80)</sup> must also be accepted with caution. Even in it the action of the heart cannot be determined with absolute certainty, although his opinion that the right auricle and ventricle continued beating regularly, while the left ventricle contracted with every second or third beat, is almost absolutely confirmed by the accompanying venous pulse tracing. Such a condition is not impossible, considering the serious changes in the action of the heart which can arise from disturbances of conductivity, contractility, and excitability.

And recently Mackenzie, who is such an expert in the study of the heart, has published examples of undoubted discordance of the right and left chambers of the heart (<sup>75</sup> Chap. XXIX.). I shall not

<sup>1</sup> Even after the most recent article by V. Leyden (*Deutsche med. Wochenschrift*, 1903 No. 23), I am not inclined to change this opinion (*cf.* H. E. Hering, *Deutsche med. Wochenschrift*, 1903, No. 3).

discuss these cases of Mackenzie in detail, but I wish only to allude to his careful and interesting analysis in order to show that certain forms of hemi-systole, or discordant action of the two halves of the heart, do apparently occur even in man; and hence we must include this variety of pulse among the clinical types of arrhythmia. It is certainly a very rare phenomenon, and does not possess the importance which was formerly attached to it.

#### PULSUS FREQUENS—TACHYCARDIA

§ 73. The rate of the heart normally depends upon the intensity of the stimulus-production and the degree of excitability, and, generally speaking, changes in the rate are due to chronotropic and bathmotropic influences. It is a well-known fact, and one readily understood, that chronotropic influences are continually at work in adapting the frequency of the heart's action to the requirements of the body (*cf.* § 51, &c.).

A frequent pulse is usually the result of this chronotropic influence. Still, an abnormally high frequency may be simulated by the appearance of numerous extra-systoles. In such a case the physiological stimuli may be produced at a moderate rate, and yet a much greater number of systoles is observed.

A special variety of pulsus frequens is seen in the excessively high frequency that comes on in paroxysms, so-called "paroxysmal tachycardia." A. Hoffmann has written an exhaustive monograph on this form of pulse,<sup>(52)</sup> and collected the literature bearing on this subject. His conclusions, as well as those in recent literature, which it is impossible to deal with in detail here (*cf.* Maixner,<sup>(78)</sup> Rose,<sup>(96)</sup> Singer,<sup>(108)</sup> and others) go to show that these paroxysms must be held to be of nervous origin. After what was said in the section on the action of the nerves on the heart, it is only possible to assume that a nerve influence is really the cause of this phenomenon, and hence these attacks of tachycardia are in a sense the reverse condition to paroxysmal bradycardia or Adams-Stokes' disease. We must, however, consider more closely the mechanism of this phenomenon.

A. Hoffmann<sup>(52)</sup> pp. 174-176) was the first to assert that in paroxysmal tachycardia the numerous beats were all extra-systoles, and not ordinary contractions. He bases this theory on the fact that after an attack, and in direct connection with it, irregularities occur which he says are due to extra-systoles, and regards the whole

attack as a kind of tetanus of the heart similar to the result obtained experimentally on tetanising the heart, the tetanus always resolving itself into separate contractions on account of the refractory phase.

Mackenzie (<sup>75</sup> p. 126, &c.) came to a similar conclusion independently of Hoffmann, and gives the following reasons: "First, that it is the only one that can account for the long-continued extraordinary rapid action of the heart; second, in many cases the rapid pulse can be demonstrated to consist of series of groups of premature systoles; and third, the attacks present certain analogies to attacks of irregular heart action, when the heart does not acquire this excessive rapidity."

I myself have never yet met with a typical case of this disease, and therefore cannot express a definite opinion on its mechanism. I would venture, however, to make some remarks on the arguments of these two authors; the first is that Mackenzie has evidently adopted the method by which we may yet be able to solve this problem in the case of man, viz., by taking tracings of the venous pulse and apex beat as well as of the radial pulse.

In the second place, it must be noted that the line of argument which Hoffmann adopts in his theory cannot be reconciled with the present views of physiologists. He is quite right in assuming a nerve influence, but that cannot well be connected with extra-systoles. Indeed, he says himself: "It is impossible to explain all the symptoms on the ground of an increased excitability of the heart alone;" and he concludes, "It must be assumed that in an attack of tachycardia not only the tonic action of the vagus is wanting, but chronotropic stimuli which are stronger than the physiological ones are continually acting on the heart." But these "chronotropic stimuli" can never excite extra-systoles directly. It is proved from all that we know that it is impossible to set up extra-systoles from the nervous system directly; instead of chronotropic stimuli we should speak of chronotropic influences due to stimulation of the central nervous system. The effect of this is that the production of stimuli is enormously increased, and physiological (not extra-) systoles are excited at a much greater rate. It is very probable that positive bathmotropic influences are present at the same time; indeed, on theoretical grounds a strong positive bathmotropic influence alone might be sufficient to produce a high frequency. Considering, however, the great importance of chronotropic influences it is more likely that

both these influences occur together. The great rise in frequency, therefore, would seem to be due rather to nerve influence. It would not agree so well with the nervous origin of the phenomenon to call all the systoles extra-systoles. If that were done one would be bound to assume an exceedingly strong and continuous extra-stimulus in addition to the positive chronotropic and bathmotropic nerve influence. It is not surprising that irregularities occur at the end of the attack, and these might be quite naturally explained by the gradual disappearance of the chronotropic and bathmotropic influences, although Hoffmann ascribes them to extra-systoles without, however, being able to prove this with certainty.

Neither are the reasons adduced by Mackenzie, who, moreover, does not look for an explanation of this irregularity from a physiological standpoint, quite valid. It is questionable whether all the systoles during the paroxysm are "premature" contractions, because he was also able to demonstrate them apart from these attacks. The tracings which he reproduces, however, show in these incompletely developed attacks groups of frequent systoles, but these present not the character of extra-systoles, but that of early occurring frequent physiological contractions produced by chronotropic influence (*cf.* §§ 77-83). Mackenzie also analysed the movements of the heart during the attack, and found (§ 211) that at that time the venous pulse takes on a "ventricular" character. He did not, however, conclude from that that ventricular extra-systoles occurred, but attributed this condition to the excessive over-filling of the auricle and the consequent paralysis of its muscular wall.<sup>1</sup>

Everything then points to the fact that it is chronotropic and bathmotropic nerve influences that produce the tachycardia. This condition therefore comes under the group of paroxysmal arrhythmias, together with the forms of excessive bradycardia discussed in § 57. From what we know of these paroxysmal irregularities of nervous origin, we may expect that paroxysmal tachycardia will occur in different forms; hence it is desirable to make a careful analysis of each individual case.

#### PULSUS RARUS—ADAMS-STOKES' DISEASE

§ 74. **Various Causes of Bradycardia.**—The name that is used to denote a slow pulse is "pulsus rarus" or "bradycardia." The former refers only to the pulse, and is therefore merely of

<sup>1</sup> *Vide* Appendix 7.

value as a collective name. The word bradycardia signifies something more, viz., that a low frequency of the heart causes the slow pulse. Now it is clear that the low frequency of the heart can arise in various ways, and therefore the name "bradycardia" does not convey any definite idea.

The most simple case is where the heart itself beats very slowly, and the heart and pulse therefore correspond. These cases are not very rare; it depends how low the rate can be and still be considered physiological. The low frequency may either be permanent or only temporary, and the cause of it may be in the heart itself as well as in other organs (the central nervous system or through reflex channels): cf. § 51, &c.

But it may also happen that the heart contracts at the normal or even at an increased rate, and yet a "rare pulse" is found at the radial. The causes of this phenomenon have already been discussed. They may be divided into the following groups:—

1. Extra-systoles, which are frequently not perceptible in the peripheral arteries, and when they occur regularly may even produce a pulse with half the frequency of that of the heart.

2. True bigeminy of the heart. When the second systole does not produce a pulse-wave that can be felt, the length of each pulse period becomes equal to the interval between each pair of systoles (*e.g.* Fig. 9, Plate II.).

3. Ventricular systoles, which drop out or cannot be felt at the periphery. In such cases the systoles drop out as the result of grave disturbance of the stimulus-conduction or the excitability:  $\frac{1}{2}$ ,  $\frac{1}{3}$ , or  $\frac{1}{4}$  frequency can then occur (heart-block). When the contractility is reduced, the weaker systole resulting from the alternating action of the heart may not be perceptible in the periphery, and therefore produce a half-frequency in the pulse.

In all cases of *pulsus rarus*, therefore, we have to decide whether bradycardia is really present, or some process is obscuring the normal frequency. Extra-systoles can be easily recognised. In a case where the frequency is reduced in a definite proportion, one would first think of heart-block.

§ 75. **Paroxysmal Bradycardia: Adams-Stokes' Disease.**—A special form of bradycardia is seen in cases where it occurs in paroxysmal bradycardia, or Adams-Stokes' disease, a form that has been analysed and described by various authors within recent years. The different varieties of this disease were discussed

in detail in the section on the action of the nerves on the heart. But clinically we can distinguish two forms, as Quelmé<sup>(89)</sup> has correctly shown: (1) the form "*à pouls lent permanent*" where between the attacks the pulse keeps at an exceedingly low rate, and during the paroxysms is still slower; (2) the form in which the pulse between the attacks rises to its normal, or even an increased frequency. The paroxysms of excessive bradycardia are accompanied by very serious nervous symptoms, unconsciousness, epilepsy, and apoplexy.

There is no longer any doubt that these paroxysms are of nervous origin, and this explanation is accepted in the more recent literature. But the nerve-influence can arise from lesions of the central nervous system as well as reflexly (*e.g.* from the heart itself). In the case of the "*pouls lent permanent*" we must perhaps assume that there are changes in the musculature of the heart.

Now, although there is a consensus of opinion about the origin of this phenomenon, authors differ considerably about the mechanism of the heart during the paroxysms. In the section on nerve influences we dealt with the extraordinary variety of forms in which it may manifest itself. Besides the most positive cases of heart-block recorded by Chauveau, His, Mackenzie, and others, there are some in which a negative inotropic or a negative chronotropic influence predominates. Hence it is not surprising that in cases of undoubted Adams-Stokes' disease the one author observed one abnormal symptom and the other another. Webster's case shows how, even in the same patient, a negative inotropic influence can be found at one time, and a negative chronotropic and dromotropic influence at another.

Such a great variety in the form calls for a thorough analysis of each case, but this does not prevent the various forms from being regarded as of common origin. The results of Engelmann's researches on the action of the nerves on the heart have taught us how apparently exactly the same nerve stimuli (reflex stimuli) very often produce very dissimilar effects. We may therefore take it as established that these various disturbances of the heart's action are of nervous origin: and hence forms that are diametrically opposite to one another, like paroxysmal tachycardia and Adams-Stokes' disease, can in a measure be included under one group of irregularities.

A thorough examination of each individual case, especially when

carried out by the excellent method which Mackenzie employs, will undoubtedly be able to throw great light on these interesting anomalies of the heart.

### THE NEUROSES OF THE HEART

§ 76. The neuroses of the heart must be taken into account only in so far as they lead to irregularities in its action. The irregularities due to nerve influence, however, have been dealt with in the section dealing with that subject as well as in §§ 73-75. The symptoms of the arrhythmia due to this influence will be found there.

Generally speaking, the name neuroses of the heart has been used with insufficient reason in too many cases when no organic lesion could be detected as the cause. It is unnecessary to repeat that this is not right. Numerous authors described extra-systoles as a neurosis of the heart. In §§ 26, 27, it was shown that general neuroses can undoubtedly favour the occurrence of extra-systoles, and in § 61a it was discussed how it may really be difficult to determine whether a chronotropic influence or extra-systoles are present. It is, however, perfectly certain that extra-systoles, occurring in a heart that shows no organic lesion, cannot at once be regarded as a neurosis.

We can only diagnose a "neurosis" in any case of arrhythmia of the heart where the arrhythmia itself bears the distinct signs of a nervous origin that were laid down in the section on nerve influences.

### EXCESSIVE IRREGULARITY—DELIRIUM CORDIS

§ 77. **The Irregular Heart.**—It remains now to discuss those cases in which the heart presents an apparently or really complete irregularity of action—cases that are often called by the name "delirium cordis."

It has long been known that such a complete irregularity of the heart has no definite significance for the condition of the heart itself. Many persons, especially those more advanced in years, enjoy perfectly good health, and are quite able for their work, in spite of a continued extreme irregularity of the heart. In old and also in younger people that suffer from organic disease of

the heart, and even in perfectly healthy, usually "nervous," individuals, these irregularities continue often for days and weeks, and then disappear again for a long time; sometimes they come on quite suddenly, in paroxysms, as the result of all kinds of injurious influences, sometimes in consequence of slight diseases, cold, auto-intoxication (constipation), &c. In these cases of temporary irregularity every physician has been able to observe the exceedingly beneficial effect of digitalis.

When we analyse a tracing of the heart's action in delirium cordis, we frequently find parts in it that present a close resemblance to forms that are at present better known. At the same time it is remarkable that different cases have a different appearance. An exact analysis of the heart in all these cases now is not of the first clinical importance, but it is undoubtedly of value as a contribution to the knowledge of the disturbances of the cardiac rhythm. Since there is considerable difference of opinion in interpreting such tracings, I shall attempt to give the full analysis of a few cases of irregular heart. I only give it as an attempt; many problems must in the meantime be left undecided.

§ 78. **Extra-Systole or Premature Systole?**—Many authors have described and given tracings of the irregular heart; among more recent writers I would specially mention the cases recorded by Mackenzie. He, like many others, observed that numerous "premature" and sometimes "abortive" (*frustrane*) contractions play a part in the production of these forms. It is therefore natural to think that extra-systoles are the cause of the frequent and irregular action of the heart. Now, in many cases it is quite easy to show that extra-systoles are actually present. In the chapter on extra-systoles (§ 19) we pointed out at some length that, though the motor-stimuli may be generated with perfect regularity, the heart may yet show the most pronounced arhythmia, because numerous extra-systoles occur at different periods during the diastole, and by thus producing larger or smaller early waves, or even intermissions in the radial pulse, simulate an irregular heart. In these cases the original rhythm can be ascertained by a careful measurement of each period, and the extra-systoles can be distinguished from the physiological beats by the definite length of the compensatory pause.

But the case is not always so easy. We frequently find the compensatory pause is not of a definite length—indeed, is absent

altogether. If in these cases it is assumed that they are extra-systoles, one is also bound to assume that they proceed from the mouths of the great veins, because extra-systoles that do so are not followed by a compensatory pause. But then we are at once met with the difficulty, which we have already found repeatedly, that when there is no pause we cannot say with certainty whether we have to deal with extra-systoles or early occurring physiological beats. With this dilemma we must look for other signs which will help us to a decision; considering the fundamental importance of this question, I cannot but lay special emphasis on the difference between these two kinds of systoles and their differentiation. Among more recent authors, H. E. Hering, when once he had observed the extra-systole in man, has too readily called all early occurring systoles extra-systoles. Mackenzie, who only speaks of "premature contractions," and has not taken into account the extraneous character of the extra-systole, has also confused the two kinds of systoles, and has emphasised only the "premature" form. Still, in future research, the difference between them must not be overlooked; and I trust we shall yet be able to avail ourselves of more exact signs than is possible at present with the analysis of several cases, which I shall now endeavour to make.

§ 79. **Cases of Irregular Heart.**—Fig. 37, Plate VII., represents a portion of a pulse tracing obtained from a woman, æt. 52 years, who suffers from obesity and fatty heart, exhibits a slight defect of compensation, and has continually an irregular pulse. When we examine this pulse in a long series of tracings, the normal length of a period in the regular parts appears to be  $\frac{17-19}{25}$  sec. In the portion reproduced here there is at 1 a small early occurring wave, followed by a period of  $17\frac{1}{4}$ . If that were an extra-systole, it would certainly be one of the doubtful kind, proceeding from the root of the heart. The next small wave is followed by too short a pause; one would therefore have to assume that, if this was an extra-systole, the next one was also the same. But it does not look like that, and besides, there is never any compensatory pause at the end of the more frequent period. Who could say which is an extra-systole and which an physiological systole here? Apart from other irregularities (periods of 22.5, 19, 21), we find at 2 a slight increase in the rate of the pulse, at 3 a slightly greater, at 4 the same, and at 5 a long series of very fre-

quent pulse-waves. The absence of any compensatory pause, and the transitions from a frequent to a less frequent pulse, oppose the idea that they are extra-systoles. On the contrary, one is compelled to assume that the original rhythm in this case is very irregular; the motor stimuli are not generated in a regular rhythm, and chronotropic influences of a myogenic or neurogenic character have an effect on the heart. Considering the high frequency, one must assume that the excitability of the heart is too high.

§ 80. One might say with more reason that there are extra-systoles in Fig. 38. This tracing was taken from a healthy old woman, eighty-nine years of age, during a slight attack of bronchitis; during this attack she exhibited an extremely irregular heart, which, however, became regular in three days, under the use of digitalis. (This patient lived for two years more.) In this case it was very interesting to note how the original rhythm became more and more apparent in the pulse as the patient improved. The length of the normal period is  $\frac{17.5-18.5}{25}$  sec. Premature contractions, and even groups of them, are continually occurring; but in contrast to the previous case, there is always a long pause after the small waves, instead of a gradual fall to a lower frequency, this pause being at least as long as, and often even longer than, the normal period. This fact favours the idea that these small systoles, although they were often produced at or near the ostia venosa, were true extra-systoles.

But there are several doubtful points in this case also.

It may be asked: Why is the first wave 1 in the group of small beats so much reduced in size, in spite of the fact that it was preceded by the longest normal period? It does not arise from an extra-systole, because the period is a normal one. We must suppose that the contractility of the heart-muscle was diminished, that a negative inotropic influence was at work, and hence the systole was a smaller. A similar case was described in § 57 and illustrated in Fig. 27. But on this supposition the nature of the succeeding small systoles becomes doubtful, for we know how often various nerve influences are combined; and in this case a negative inotropic and a positive chronotropic influence are possibly combined, similar to what we found in § 60. Still we cannot exclude the possibility that extra-systoles may be present along with a negative inotropic influence. This anomalous case only

shows how careful one should be against rashly jumping at conclusions.

§ 81. In dealing with the influence of the nerves on the heart, we repeatedly alluded to the simultaneous disturbance of several functions. Fig. 39 *a* and *b* shows a tracing in which such a condition must be assumed. It was shown to me some years ago by Prof. Rosenstein in Leyden, because there were no corresponding pauses to the extra-systoles which were present. The tracing was taken from a man *æt.* 45 years, who was suffering from degeneration of the myocardium.

This form of pulse is very frequently met with, and hence it is of some considerable interest to give a proper explanation of it. The same question arises: Are the small waves extra-systoles or physiological systoles? When we have only the sphygmogram to look at, we must see whether we can find extra-systoles interrupting the normal rhythm; but they do not. It is true, a long pause can often be seen at the end of a group of frequent small waves, *e.g.* in Fig. 39 *a* at \*. But the rhythm of the heart itself is extremely irregular, and at the commencement of this figure the length of the pause after what seems the first extra-systole does not at all correspond to the rhythm of 6.5. The rest of the pulse also shows extreme irregularity. It would be very bold to say there are extra-systoles here, when we see in Fig. 39 *b* how a group of small and more frequent waves passes into the slower rhythm without any pause. I cannot therefore see that extra-systoles are the cause of this irregular pause, and believe that, until we acquire more experience, we are bound to assume in this case a great irregularity in the rhythm of the heart, together with marked chronotropic and bathmotropic variations. Whether the changes in these cases are of a myogenic or neurogenic character must still remain an open question.

§ 82. In cases of irregular heart definite types can often be observed, and in the same case even different types at different times. An example of this was seen in the pulse of a female, *æt.* 75 years, who suffered from well-marked sclerosis of the heart and vessels. In a tracing taken when the patient was in good health the period length in the regular parts of it varied from  $\frac{15-18.5}{25}$  sec. In the part here reproduced (Fig. 40 *a*), we see several groups of small waves. Are these groups of extra-systoles? Only twice do we find

a normal period of 18 and 18.5; all the others have shorter periods. If they were extra-systoles proceeding from the vena cava, we would be bound to meet the normal period or longer pauses much more frequently. Hence it is much more probable that there is an irregular increase in the rate of the pulse. We are therefore forced to assume chronotropic, and perhaps also bathmotropic influences.

In other tracings which were taken from the same patient during attacks of dyspnoea, other influences became apparent besides the chronotropic; Fig. 40 *b*, *c*, and *d* were taken at this time. Groups of small systoles still show themselves, as is seen in *b* and *c*, but the rate of the pulse generally was higher, a normal period measuring now only  $\frac{13-15}{25}$  sec. If we examine these groups more closely, we find that the first wave of a group following a normal period is distinctly shorter than that period. This condition cannot be due to an increase in the rate of the pulse, but must be caused by a weaker or smaller systole, *i.e.* by a negative inotropic influence. The rate increases, the height of the waves falls considerably up to the middle of the group, after which the length of the period and the height of the wave rise again together; *i.e.* the positive chronotropic and negative inotropic influences subside. It is proved that the diminution of the pulse-waves is due not only to the increased frequency, but also to a primary weakening of the systoles, by the fact that the first wave of the group after a normal period is considerably reduced in size. This negative inotropic influence, which manifested itself before the positive chronotropic, is quite obvious in other parts of this tracing. In Fig. *b* a similar group begins at 2, but is much less pronounced. In Fig. *d* the reduction of the pulse-wave at 1 strongly suggests a negative inotropic influence, but there might be other causes for the falling out of the systole, as was explained in the section on the influence of the nerves on the heart. Still it is remarkable that the end of such groups of shorter periods with diminished systoles is often exactly like "Bowditch's staircase." In Fig. *b* as the pulse becomes again slower at 1 and 2, the tracing somewhat resembles a staircase; but in Fig. *c*, as well as in several other places throughout the pulse tracings of this patient (which could not all be reproduced), this staircase phenomenon is very well seen. As was fully discussed in § 60, this staircase is due to a restoration of the contractility of the cardiac muscle such as occurs after the long pauses induced by stimulation of the vagus, and after

negative inotropic influences. The tracing from Webster's case, that is given in Fig. 33, is an example of this.

We see therefore that extra-systoles cannot be demonstrated in this tracing, but, on the other hand, there are numerous changes in it that strongly suggest the presence of a nerve influence.

§ 83. The last example of irregular heart which I give is illustrated in Fig. 41. It was taken from a woman, 81 years old, who was exceedingly healthy for her age, and had never shown any symptom of cardiac affection. One day she suddenly complained of shortness of breath and palpitation. She had then a very irregular pulse, but under the use of digitalis this irregularity entirely disappeared again in three days.

As the figure shows, the pulse is very frequent and irregular. Long stretches of waves of equal length cannot be seen, and this gives the impression that extra-systoles occur very often. On measuring the periods and the height of the waves, we find that they are not extra-systoles, but early occurring physiological systoles. There is nowhere any sign of a compensatory pause after the small waves. Considering the great irregularities and the high frequency one would first think of positive chronotropic and bathmotropic influences, although negative inotropic changes like those we saw in the previous cases can also be observed. They are not merely the result of the high frequency or premature occurrence of the systoles, they are primary in character. If we look at the tenth and twelfth wave in the tracing, we see that the former follows an abnormally long period and is very small, although we should expect it to be larger than normal; the latter is very large, in spite of the fact that it follows two systoles which came in quick succession. If the irregularity of the periods in which these two systoles occur is observed, it will be found that most probably a nerve influence is present here also, producing very different effects.

§ 84. These examples serve to show that we cannot yet assume that all small imperfect systoles are extra-systoles, but that, while each case must be considered on its own merits, we must beware of making generalisations too readily.<sup>1</sup> These cases of irregular heart are best calculated to test our methods of analysis; and, moreover, they provide material of great value for the further study of the pulse, because the influence of drugs, and of digitalis in particular,

<sup>1</sup> *Vide* Appendix 8.

can often be very plainly demonstrated in them. One is frequently able to observe how the normal rhythm more and more takes the place of the abnormal until it is finally completely restored.

A careful analysis of all the cardiac changes that can be observed clinically will therefore not only give us a fuller insight into the disturbances of the functions of the heart, but will also open out new fields towards which future physiological and pharmacological research may be directed. I hope that this work will prove of help in this direction.

## APPENDIX

1. (§ 17, p. 41.) Dr. Mackenzie has kindly informed me that, on looking over his tracings of this case, he was able to prove from the venous pulse-tracings that my view is the right one.

Dr. O. Pan, of Prague, has reported a similar case, but he makes no mention of the case I recorded in 1899. (*Deutsches Archiv für Klinische Medizin*, Bd. lxxvii., 1903.)

2. (§ 26, p. 56.) Now that Mackenzie has demonstrated (*British Med. Journal*, 5th March 1904) that in many cases the rhythm of the ventricle determines the rhythm of the heart, it becomes more urgent than ever to consider whether the cause of this predominant action of the ventricle may not possibly be found in an increase of its automatic movement, in the sense of Engelmann, rather than in the presence of so strong extra stimuli, with or without an increase in the excitability of the ventricle.

It would be very desirable to obtain the results of experimental research on this point; in this connection a recent paper by Engelmann on Stannius's experiment (*Arch. f. Anat. und Physiol.*, 1903, p. 505) may be here mentioned.

3. (§ 35, p. 93.) The above-mentioned article by Engelmann on "Stannius' Versuch" gives a clear insight into the mode of action of the ventricle after its connection with the auricle has been lost.

Since the publication of my book, D. Gerhardt of Strasburg has described a case of heart-block, and given tracings in which periods of total heart-block were recorded.

4. (§ 37, p. 96.) A counter-theory put forward by Hering is fully discussed in the following pages, and refuted. Since my book was published, however, my views have been proved to be correct, and will receive additional proof from an article by Mackenzie on a very striking and similar case (which is about to appear in the *Deutsche Med. Wochenschrift*); although, therefore, this discussion may now seem superfluous, it has nevertheless been inserted here as in the German text.

5. (§ 42, p. 117.) It appears from a review which Hering wrote on this book that this author has now himself recognised a case of true alternans.

Dr. Mackenzie has kindly showed me some most convincing tracings of alternating heart-action, where the small pulse-waves occurred in different situations between the large waves.

6. (§ 68, p. 167.) In a recent paper, Hering described some cases of more or less continuous "bigeminy"; in one of these the constant relation between the two linked beats was not altered by an increase in frequency

that was induced by the injection of atropine. This fact seems to support my view that the two beats are really *linked* together, that the second beat is not a common extra-systole, but that the first systole *causes* the second one. (*Deutsches Archiv f. Klin. Med.*, Bd. 79, p. 175.)

Volhard recently communicated a case of bigeminal action of the heart, where the nature of the second beat could not be explained with certainty; it is doubtful whether the second beat was an auricular or a ventricular contraction. (*Zeitschrift für Klinische Medizin*, Bd. 53.)

7. (§ 73, p. 177.) A. Hoffmann has modified his views on this subject, as is seen from his papers in the *Deutsches Archiv f. Klin. Med.* (Bd. 78, p. 39), and *Deutsche Klinik* (1903, p. 155). It is obvious that the cases which Hoffmann and Mackenzie describe really belong to a very different type; so it will be necessary to avoid generalising, and to try to give an explanation of each individual case; that a ventricular rhythm may play a *role* in many cases is a fact now well established by Mackenzie; whether this occurs in the cases called "paroxysmal tachycardia" by Hoffmann seems very doubtful.

8. (§ 84, p. 186.) The above-mentioned paper by Mackenzie (*B. M. J.*, 5th March 1904) is of the utmost importance for the analysis of these cases of excessive irregularity. Still there may be some doubt about the true character of many of the beats, which Mackenzie calls "ventricular," and further research into this matter is urgently needed.

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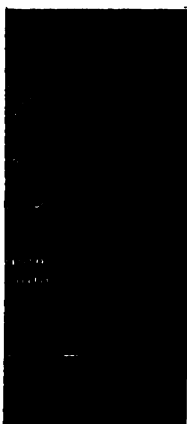
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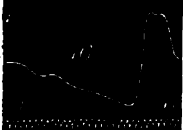
**Fig.1.**



**Fig.2<sup>a</sup>**



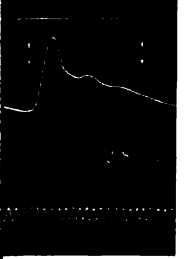
**Fig.2<sup>b</sup>**



**Fig.3.**



**Fig.4<sup>a</sup>**













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